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ILLHEALTH AND HISTORY*

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It is common knowledge that indifferent health, whether physical or mental, affects not only a man's capacity for work but also his judgment. In studying the history of any country one is struck with the fact that many famous men, and women too, had they enjoyed good health might have taken decisions which would have saved them from much unhappiness, and the nation from serious crises. It is, also, quite possible that the whole course of history might have been changed had not disease dogged the footsteps of some great statesmen and Generals.

It has occurred to me that it may be of some interest to you if we study for a brief time the lives of some famous people from a medical standpoint, and try to interpret in terms of illhealth the cause of many of their actions.

Disease is often the deciding factor in determining the course of war, and many an epidemic has brought a besieged people to their knees.

The first epidemic in war of which we have detailed knowledge is the great plague of Athens, in the Peloponnesian campaign, about which there can be very little doubt, for it is described by one of the greatest literary artists of Greece, who saw it with his own eyes and suffered from it. Thucydides was not a doctor, but he gave a remarkable description of the plague and its effect upon the people in the city, their ungovernable terror, the powerlessness of the doctors, the abandonment of all moral laws, the wild accusations of poisoning by enemies, (history has repeated itself in Korea) the selfishness, cowardice and ignorance of man in a panic, the hysterical dancing in the shadow of the tomb: and Athens fell before the enemy.

There are some who believe that Thucydides was describing not bubonic plague but Typhus fever, which has always been the enemy of besieged cities, especially in hot and dirty surroundings. Dr. Crawford is of opinion that the plague of Athens was undoubtedly Typhus.

During the First World War I was at Gallipoli. The incidence of dysentery and Typhus was so great on the right of our line, Cape Hellas, that for a few weeks, had the Turks been aware of the situation they could have driven us into the sea without firing a shot. The proverbial good luck of Great Britain prevailed.

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The great plague of the Antonines was probably the real cause of the decline and fall of the Roman Empire. Unfortunately Galen, the Roman Hippocrates, ran away from it. Doctors now-a-days have the courage to continue their work in the face of the worst epidemics.

Disease throughout the middle ages was rampant and, in spite of the glamour that enthusiasts and romanticists have cast upon that period of the world's history, most people will agree with Sydney Smith when he wrote:

"The good of olden times let others state,
I think it lucky I was born so late."

When the Empress Isabel was pregnant with the child which was to be Philip II of Spain, she bethought her of the glory that was hers in bearing offspring to a man so famous as the Roman Emperor and she made up her mind that she would comport herself as became a Roman Empress. When, therefore, her relations and midwives during the confinement implored her to call out or she would die, the proud Empress answered, "Die I may, but call out I will not," and thus Philip arrived in the world the son of a stoical mother and a heroic father. The calamity of his life was that his father had bequeathed to him not only the kingdom of Spain but also that of the Netherlands. To the Netherlanders Philip was a foreigner, and so the Dutch rose in revolt under William of Orange and formed a republic. Philip saved the Southern Netherlands from the wreck and this ultimately became the kingdom of Belgium. Philip, in order to get England on his side, married Mary Tudor, a woman twelve years older than himself, but this diplomatic marriage did not conceive the desired result. Hence Philip's attempt to conquer Great Britain by the Armada. Philip was austere in his mode of life and always had a Doctor at his side at meals lest he should forget his gout. He lived abstemiously, but took too little exercise. It would have been better for his health and probably for the world had he followed his armies on horseback as his predecessors had done before him.

In the well-known picture of him receiving a deputation of Netherlanders, as he sits in his tall hat beneath a crucifix it is evident he is wearing a large, loosely fitting slipper and suffering tortures from gout. These unfortunate gentlemen seem to have selected the wrong moment to ask favours, for there is no ailment which so warps the temper as gout. What justice could they have expected to receive from a man tortured and rendered petulant and gloomy with gout and diabetes?

When we consider that the destinies of nations are commonly held in the hands of gentlemen whose blood pressures are too high, it is not too much to say that arterio-sclerosis is one of the greatest tragedies that afflict the human race. It has been stated that every politician should have his blood pressure tested and his urine examined once a quarter, and if neither is normal he should be forbidden to make a speech until the next quarter's examination.

In view of the present heavy taxation, this increase in doctors' incomes from having all our politicians as patients would be very welcome.

The wife of Philip of Spain, better known as "Bloody Mary", had always been a sick woman. As a girl she had suffered from menstrual troubles. Soon after her marriage she became pregnant and miscarried. The disappointment weighed heavily on her mind, so much so that she developed pseudo-cyesis, a condition in which the abdomen becomes distended

and simulates pregnancy. She was very shortsighted, and—as Sir Clifford Allbutt pointed out—this may have been due to interstitial keratitis, an affection of the cornea of the eye which is almost confined to hereditary syphilitics. Is it not possible that her poor health was partly responsible for her acts of persecution during her short reign?

Let us now turn to a study of the medical history of her father Henry VIII. So much has been said and written about this notorious King of England that it might seem a waste of time to probe still further into his life. There is little doubt that he suffered from syphilis and handed on the disease to his wives and children. The actual number of premature births endured by these women is in dispute, but there were more than can be accounted for by any disease other than syphilis. It is probable that three of his children had constitutional syphilis, Mary Tudor, Edward VI, and the illegitimate Duke of Richmond. Whether Queen Elizabeth escaped the infection is also at least doubtful.

As regards Henry VIIIth's health the British Medical Journal of 1910 states: "From being an able and athletic man he had become a mass of loathsome infirmities. He was bloated in face and so unwieldy that he could hardly pass through an ordinary door. His legs were swollen and covered with festering sores causing an unbearable stench. He had a sinus in his leg which may have been caused by Syphilitic Periostitis."

Henry VIII died at the comparatively early age of 55. In syphilis and self-indulgence we have the secret of the whole tragic development of this King's character. While there are not sufficient details to offer an opinion, it is possible that at the end of his life he became uraemic, due to the slow degeneration of his kidneys. Had he been living in this generation some Canadian or British urologist might have saved his life.

Many are the slanders that have been passed upon that extraordinary daughter of Henry VIII, Queen Elizabeth. Professor Pollard, whose meticulous fairness will absolve him from any conscious bias, sectarian or otherwise, writes as follows concerning her amazing juggling with her numerous suitors:

"There is evidence that she had no option in the matter and that a physical defect precluded her from hopes of issue." On this supposition her conduct becomes intelligible, her irritation at parliamentary pressure on the subject pardonable, and her outburst on the news of Mary Stuart's motherhood a welcome sign of genuine feeling. You will remember that when she heard of the birth of King James I to her rival Mary Queen of Scots, she said with bitterness, "The Queen of Scots is the lighter of a fair son, but I am a barren stock."

Possibly there was a physical cause for Elizabeth's masculine mind and temper, and for the curious fact that no man lost his head over her as many did over Mary Queen of Scots. To judge from the portraits Mary was as handsome as her rival, but apparently Elizabeth had no feminine fascination and even her extravagant addiction to the outward trappings of her sex may have been due to the absence or atrophy of deeper feminine feelings. The impossibility of marriage made her all the freer with her flirtations and she carried some of them to lengths which scandalized a public unconscious of Elizabeth's real security. Her amazing personality is best explained by endocrinology. Sometimes she seems to have had all the male qualities, such as swear-

ing, roughness of speech, freedom from convention. Sometimes she behaved like a doting old maid in her inordinate love of dress, jewelry and flattery. Her endocrine balance was abnormal.

For the four years preceding the battle of Waterloo it is well known that Napoleon was far from well. He suffered from difficulty and frequency of micturition and, in view of the post mortem findings at St. Helena in 1820 when stones were discovered in the bladder, I think we are correct in our surmise that they must have been present many years previously. It is rather surprising that nobody suspected it during his lifetime, but it must be remembered that surgeons in those days, especially the army variety, were ignorant and incompetent. Also Napoleon's well known intolerance of the medical profession and his all powerful position in France, possibly prevented his doctors from daring to suggest that he had a disease which required surgical treatment. Yet he had admired Baron Larrey, probably the most famous of the surgeons of the Napoleonic wars. One can only surmise that his great strength of will kept under control his commencing physical infirmities, but it did not prevent him from making mistakes.

At the battle of Borodino in 1812, the bloodiest of all battles to date, Napoleon, it is true, won and the Russians retreated to Moscow, but he lacked that supreme genius which he had displayed in his other campaigns. In 1815, the year of Waterloo, he had defeated Blucher at Ligny, but instead of furiously pursuing his defeated foe, as had always been his wont, he wasted precious hours in lethargy.

Would he have won the battle of Waterloo had he not suffered from ill-health? To this day there are Frenchmen who answer that question in the affirmative. Four years later Napoleon was dead of cancer of the stomach. The bladder contained gravel and several definite calculi.

In 1870, the Prussians had their revenge on France for Napoleon I's victories over fifty years ago, and by their peace terms in which Alsace and Lorraine were handed over to Germany sowed the seeds of the great European War of 1914-19. Napoleon III was a sick man when France declared war on her hereditary enemy in 1870, but it is doubtful whether even had he enjoyed good health he could have saved his crown and his country. The French army was thought even fifty years after the death of the great Napoleon to be still the finest in Europe. Napoleon III at the outbreak of war tried to lead his army into the field but he suffered so much excruciating pain when riding his horse that he had to return to Paris. The moral effect of this on the French army was disastrous.

When he had lost all, he fled to England, and there the late Sir Henry Thompson, a surgeon with a great reputation for the treatment of diseases of the urinary organs, crushed the stones in the ex-King's bladder, which had caused him so much pain.

The history of the building of the Panama Canal is full of tragedy. De Lesseps, one of the greatest geniuses this world has produced, having been successful in building the Suez Canal in 1869, turned his attention nearly twenty years later, at the instigation of a group of French financiers, to that narrow strip of land in Central America known as the Panama Republic. In 1887 work was commenced at Colon, a town on the Atlantic coast of Panama, to make a

canal which was to unite the Atlantic and Pacific oceans. We are not concerned here with the financial aspects of this engineering feat and what are known as the Panama scandals, suffice it that disease alone ruined De Lesseps' efforts. He had not reckoned with the pestilential swamps through which he proposed to build his canal. It is of historical interest that De Lesseps' plans in toto were successfully carried out by the United States of America thirteen years later. In spite of financial difficulties, this amazing engineer would have succeeded in building this canal had he considered the health of the thousands of navvies and other workmen needed for his project. They died, not in tens but in hundreds and thousands, from Malaria and Yellow Fever.

In 1900, the United States Government before sending a single man to this mosquito infested country sent a Commission to study Yellow Fever in Havana. By this date it was known how man contracted Malaria through the bites of a certain type of mosquito. Could the same be true in the case of Yellow Fever? The American Commission at Havana erected a hut of two compartments, separated by a fine meshed wire screen. In the one compartment were mosquitoes infected from a case of Yellow Fever: their infectiveness had been proved by a voluntary act of self experiment. The volunteer died from the disease. In the other compartment men slept in contact with clothing, sheets, linen soiled with blood or vomit from Yellow Fever patients. These experiments went on for twenty-one days. The men took no harm. When they had thus disproved the old belief that the fever can be transmitted by contagion, they exposed themselves to the mosquitoes and all of them got the fever. Thus by 1901 the case against the mosquito was complete. As Anopheles conveys malaria from man to man so Stegomyia conveys yellow fever from man to man. Commencing in February, 1901, orders were issued in that part of the Panama called the Canal Zone that every suspected case of yellow fever should be screened with wire gauze, so as to render the room or rooms mosquito proof. At the same time all the mosquitoes in the infected house were destroyed.

After the middle of February, men were employed in carrying out the destruction of the mosquito-larvae in their breeding places, putting oil in the cesspools of all houses, clearing the streams, draining the pools and oiling the larger bodies of waters. By the end of September the last focus of the disease had been got rid of. For the first time in the history of Panama she had been freed from Yellow Fever.

When I visited the Panama Canal Zone in 1909, I was deeply impressed with the healthy appearance of the navvies and the organization set up to maintain the public health. Had De Lesseps realized the importance of this, the successful outcome of his project would have been assured in 1889. During the Hitler regime Fascist newspapers used to tell us that the axis front was the Panama Canal. This of course could not be taken seriously, but were a foreign army to set foot in the canal zone germ warfare could be as effective as bullets and bombs in destroying it.

To come to more recent times, one is perhaps permitted to wonder what would have happened to Great Britain politically if Joseph Chamberlain had not suffered from gout and arterio-sclerosis. Some of you will remember that in 1903

when he was Colonial Secretary, and after a visit to South Africa, he launched the campaign of tariff reform and preferential treatment for the Dominions and Colonies at the expense of the foreigner. This is the description of the great statesman given by H. A. L. Fisher the late Warden of New College, Oxford.

"The Prophet of Tariff Reform, trim, beautifully dressed, an orchid in his buttonhole and a monocle in his eye, toured round the country expounding his views with incomparable vigour, now appealing to imperial sentiment, now pointing to the increasing severity of foreign competition and in particular to the advance of German industry, and then followed him Asquith, the brilliant spokesman of the Free Trade Liberals. The Unionist Party was split and weakened by the secession of the Duke of Devonshire and Goschen." How well do I remember the discussions in my own family as to who would win, Chamberlain or Asquith. But the crash came with the usual suddenness. Chamberlain was seized with apoplexy. A haemorrhage into the brain left him speechless and paralysed. Never again was he to address an audience on tariff reform. The reformers had lost their leader: a ship without its rudder.

Free Trade had won the first round but it had no staying power and Dominion and Colonial Preference gave it the knock out blow at Ottawa in 1932. One wonders if Joseph Chamberlain's health had not failed him in 1903 whether he would have won over the people to his point of view before the general election of 1905. Who can say?

The megalomania of Hitler and Mussolini has caused controversy, and much speculation about the normality of their mental state of health. During the first and second decades of this century syphilis was prevalent in Germany and Italy, and it has been hinted that the spirochaete was busy in the brains of these men, stimulating them to perform acts of self aggrandisement.

There is no evidence that either suffered from this disease, for an overweening ambition is not necessarily a sign of mental ill health. Were it so many politicians and even members of my profession would be certifiable.

The greatest asset to any man is good health. The campaign in every country for national fitness is directed to the younger generation. A healthy mind in a healthy body is equally needed for the leaders of all nations.

Some of the information in this lecture has been obtained from McLaughlin's "De Mortuis" for which the author wishes to make acknowledgment.

I bless God I have never been in so good plight as to my health . . . these ten years as I am at this day. But I am at great loss to know whether it be my hare's foote, or taking every morning of a pill of turpentine, or my having left off the wearing of a gowne.

SAMUEL PEPYS

NORMAL PELVIC MORPHOLOGY AND OBSTETRICAL LABOR

JAMES C. GOODWIN, M.A., M.D.*

One of the more important advances in the science of obstetrics in the 20th century is the acceptance by obstetricians of *first*, the concept of normal morphological variations in female pelves; and *secondly* the variations in the mechanism of labor which relate to these morphological pelvic types. It is reasonable that a further and significant advance may be concerned with the importance in labor, of the relation of foetal cephalic morphology (i.e. foetal head shape) to the normal variations in maternal pelvic morphology. To reiterate, one must consider variations in the adaptation of the foetal head to the mother's pelvis by reason of the *shape* of the child's head, not just by reason of its size or volume.

Now let us move back to forgotten centuries in a search for the early development of foetal and pelvic morphological concepts in obstetrics. Hippocrates has been given the credit in the 4th century B.C. for making the first comments concerning the adaptability of the female pelvis in labor. His observations in all probability were based on a rather casual viewing of dry female skeletal material. It was possibly from this that he made a statement which was held as an almost absolute law by those interested in the anatomical and obstetrical sciences until toward the end of the 16th century; i.e., for approximately 1900 years. Hippocratic authority stated that the pelvic bones during childbirth underwent an actual separation (presumably at the joints) to permit the passage of the child. Next, Soranus in the 2nd century A.D. suggested that a narrow pelvis was a cause of difficult childbirth, but attributed the dystocia to the failure of the pelvic bones to separate, in keeping with Hippocratic dogma. The science of anatomy made little progress until the 16th century: attempts to improve the accuracy of anatomical study of the pelvis being disregarded in favor of mere repetition of knowledge from traditional sources. The first English book on Obstetrics "The Byrthe of Mankynde" (in the 16th century) added nothing to the knowledge of pelvic anatomy. Herein we find—"Among the perylles and daungers which chaunce to Women in their labor", this book mentions as a cause of difficulty, "when the passage be over anguished, streate or narrow, either naturally or els for some disease and infirmity". The writer in his use of the term "naturally" *almost* rings a "normal pelvic morphological" bell in the 20th century! Difficulty in labor however, was attributed by him once more to pre-existing ideas; and any hope of obstetrical advance at this time was again lost. It remained for Vesalius in 1543 to give the world the first correct description of pelvic anatomy. He claimed the impossibility, due to pelvic anatomical structure, of actual bony separation in labor.

The Hippocratic dogma died a slow

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Based on a University of Toronto postgraduate lecture, September 1952.

death; though the majority of physicians accepted the anatomical observations of Vesalius. This concept of the pelvis as an unyielding bony channel in labor persisted until about the end of the first quarter of the 20th century. Over twenty years ago in this department, (Obs. & Gyn., U. of T.) evidence was found by radiological and pelvimetric methods that separation of the pelvic bones *does occur* in pregnancy, and possibly further during labor: especially at the symphysis pubis and the sacroiliac joints. This was found to occur by reason of actual joint softening and increase in joint width; thus leading to increase in certain diametric measurements, and permitting increased pelvic joint mobility in labor. The experimental work of Hisaw suggested that the cause of joint softening lay in the production, during pregnancy, of what he termed the hormone "Relaxin"—a fraction of the corpus luteum hormone. It is questionable if the production of this hormonal fraction is constant, as all the pelves we studied did not demonstrate equal evidence of joint widening; and joint relaxation was less a feature in pregnancy as age progressed: especially in the primigravidae of over 38-40 years of age. Perhaps this historical digression will be of interest when we consider below, the adaptability of the pelvis in labor. Joint relaxation is *definitely* one factor which assists in overcoming certain, even if only slight, foetal-pelvic morphological and capacity differences during childbirth.

However, to return to the development of the modern concepts of pelvic morphology. Although, as stated, from the time of Vesalius onward, while many physicians still maintained the bony pelvic separation theory in labor, difficulties in parturition began more and more to be related to certain poorly formed and unusual pelves. Mauriceau, in 1694, noted for the first time, certain differences between male and female bony pelves. "There is", he stated, "a larger empty space and capacity of the female pelvis." Van Deventer in 1701 wrote a book for midwives, in which for their edification, he presented anatomical plates of the female pelvis: and included a chapter on "ill forms of the pelvis that may hinder childbirth." He also stated that "a narrow pelvis" was one that, considering the proportion of the female body, was too small. He did not attempt pelvic mensuration, but suggested that the first thing the midwife should do was "to try the woman by touch, before the womb and infant are fallen down into the pelvis"—and "that she may diligently inquire how the entrance of the pelvis is formed, so she is to continue her work." Elsewhere he describes the method of "trying by touch" as "being nothing else than to pass the forefingers of either hand through the private parts into the vagina . . . being first anointed with fat, butter or oil." (Quotation from the English translation, 1716.)

The first attempt to record pelvic measurements, was undertaken by Smellie, who in his treatise on Midwifery in 1752, gave those for the "normal and the abnormal" pelves. He also described, albeit rather vaguely, the axis and inclination of the pelvis. He was the first to describe the diagonal conjugate, as a practical method of evaluating the obstetrical conjugate diameter—a method which after 200 years still dies a slow death, being of definitely limited and rather doubtful value. Essentially, however, Smellie, recognized narrow and distorted pelves as a cause of difficult labor, comparing the various pelvic measurements he obtained

with what *he considered to be a normal type of pelvis*. This viewpoint has remained unchanged in the science of obstetrics: i.e., the concept of normalcy or abnormalcy of size, not morphology, as influencing the difficulty or duration of labor. Such teaching persists even until the present day in some, though a diminishing number of obstetrical centers. Morphological studies in such centers still are concerned with the detection of the normal vs. the abnormal or contracted pelvis:—*still* following the old morphological ideas of Van Deventer (1701), Dionis (1718) and Smellie (1752)—e.g. "squat women, mis-shapen, crooked women with one hip higher than the other," pelvic distortion due to rickets, disease and bodily maldevelopment, etc., which has been stated to exist as the main factor responsible for the production of difficulty in childbirth.

Countless manual and instrumental methods of pelvic *diametric* mensuration arose in the attempt to determine clinically the normal and the abnormal. These methods occupy the textbooks of the latter part of the 18th, and all of the 19th century, and for that matter they are *still* being ground out by certain die-hard medical mills, though now radiological methods are used to measure them more accurately. The late 18th and the 19th century concept of a normal pelvis was one that would permit the delivery of an averaged sized child without undue difficulty; if it did not, the cause was sought for in the narrowing of certain diameters, notably the anterio-posterior of the inlet and the transverse (bi-tuberous) diameter of the outlet. The mid-pelvis was little stressed, and the shape of the pelvis at various planes was considered of little practical importance.

Anthropologists however had, as long as 125 years ago, indicated the way to modern progress in the obstetrical field, but the majority of obstetricians, until about 25 years ago, politely but firmly closed their eyes to anthropological studies. Stein in 1825 was one of the first anthropologists to recognize among other things, pelvic form in human skeletal material. His classification was based largely on the shape of the pelvic inlet and he distinguished four types:

1. Elliptical, with the greatest inlet diameter anteroposteriorly.
2. Round, with the inlet diameters approximately equal.
3. Elliptical, with the greatest diameter transversely.
4. Blunt, heart shaped.

Anthropological investigation showed that certain of these pelvic forms tended to occur preponderantly among certain racial (biological) groups of the people of the world. These scientists as a rule described them in relation to the whole physical pattern of the particular group of people, or the human skeletal material studied. The anthropologist Turner, in 1885, proposed a morphological classification of human pelves.

1. Dolichopellic—pelves in which the anteroposterior inlet diameter exceeds the transverse diameter.
2. Mesatipellic—pelves in which the anteroposterior inlet diameter and the transverse are of more nearly equal length.
3. Platypellic—pelves in which the anteroposterior inlet diameter is less than the transverse diameter.

A later addition was made by Thoms, the Brachypellic type—in which the inlet was more oval than the mesatipellic.

Stein's fourth group, the *blunt heart shaped form* (i.e. android) might well have been added to Turner's classification, as it was a recognized pelvic form; but anthropological inlet measurements were concerned mainly with the antero-posterior and transverse diameters. The *variations in shape* were carefully subdescribed and classified as stated, as a characteristic of the particular human racial (biological) type studied. It is of importance to give credit to such anthropological studies. These clearly showed that the majority of the differing pelvic forms *were not due* to disease or maldevelopment, but rather were normal racial or biological patterns—i.e. normal human growth variations.

Caldwell and Moloy, the first to receive publicity in the obstetrical field for their pelvic morphological classifications, might well have included in their writings, a contemporary statement referring to racial differences in human female pelves made by E. J. Carey, (Obstetrics and Gynaecology, Vol. 1, Chap. 1, p. 3, edited by C. H. Davis) that "anthropological studies will be of more practical interest, when there is included a study of the head shape and size of the infants that are born through these pelves." A combined anthropological and obstetrical investigation was undertaken in this department (Obs. & Gyn., U. of T.) commencing in 1929-30. This was done for the purpose of obtaining anthropometric measurements (including the head shape) of infants 10 days old, together with similar measurements of the mothers and fathers of such infants; and then correlating such anthropological data with the duration or difficulty of labor. This work suggested that the tendancy for easier labor occurred where the mother showed racial (i.e. physical anthropological) similarity to the father; and that following delivery the child showed this parental cephalic morphological similarity also. This work confirmed observations which have been made by anthropologists for many years. These however, were made in primitive areas where marked physical anthropological similarity existed between males and females in the racial group, and therefore in those who mated. It was our wish following our original investigation for a combined pelvic radiological, anthropological and obstetrical study, but unfortunately this was not able to be continued at that time due to the pressure of other work. This is mentioned simply to put the matter on record.

Such, therefore, is a little of the anthropological background of the origin of the modern pelvic morphological approach to the problems of labor. Notwithstanding the more or less general acceptance of the pelvic morphological classification first published by Caldwell and Moloy in Oct. 1933, there is still a die-hard peristence, demonstrated to this day, in relating the problems of difficulty or prolongation of labor to the pelvic diametric size, pelvic plane areas, pelvic volume, etc., *of the maternal pelvis alone.*

Consideration, however, has been given for some time to radiological methods of measurement of foetal skull size, notably the bi-parietal diameter, and the skull volume; *normal foetal head shape variants still being considered of impractical interest.* One may venture to suggest that further obstetrical progress can be made when the shape, as well as the size of the foetal head is taken into consideration. Such, I believe, will be a further contribution of radiology—to produce radiographs in which such may be determined with accuracy. Human

head form has been a matter of intensive anthropological study during the past century. The terms dolichocephalic (long head), mesaticephalic or mesocephalic (intermediate shaped head), and brachycephalic (round head) are accepted terminology, and may be used, with minor modification, as a foetal head shape classification.

As stated earlier in this paper, the concept of the effect of human racial (biological) admixture in the production of ease or difficulty in labor is not new. Difficulty has been related to the mixture of *different* racial types (anthropologically classified). To repeat, such has been suggested in anthropological studies for a hundred or more years. References in these studies may be found concerning ease of labor in relatively unmixed human racial groups, and the converse as well. Maternal mortality rates of different countries of the world, (prior to the introduction of sulfonamides, antibiotics, blood transfusion, improved obstetrical technique, including the use of forceps, caesarian section, etc., and better analgesic and anaesthetic methods) were highest in the U.S.A. and Canada—centres of perhaps the greatest melting pot of diverse human racial types the world has seen in the past century.

Most obstetricians are familiar with the morphological studies of Caldwell and Moloy, and other than a brief review will be unnecessary. In a roentgenological study of over 3000 female pelves, in 1941, they stated that in not more than 2% could a recognized cause such as disease, maldevelopment or trauma, account for the form of the pelves found. Thus in 98%, the pelves morphologically, must be considered as normal growth variants.

Realizing the possible complexity of these normal growth variants resulting from admixture of differing human racial types, one can recognize the difficulty that exists in attempting to classify female pelves into three or four types. The study of human genetics may account for the mixed pelvic types observed, but so far has been unable accurately to predict them. The female pelvis may in itself show the inheritance of *at least* two of the so-called 'parent' patterns delineated by Caldwell and Moloy. Undoubtedly pelvic inheritance may be even *more* complex. Such then is the problem of classification. It is only logical to observe a group of pelves generally, and then endeavour to determine which pelvic types or patterns occur more frequently. Earlier anthropological studies were confirmed radiologically as might be expected by Caldwell, Moloy, and others. They stated that there tended to be *four main groups* discernible—the so-called pure or parent morphological types as labelled by them, together with certain mixed pelvic types. Their classification intelligently must take into consideration body form, and bony characteristics as a whole: but for their purpose the denomination of the pelvic type is made from the shape of the inlet. These four parent types have been termed:

1. Gynecoid—found in North America in an approximate frequency of 45-50%; (the so-called normal female pelvis of older textbooks).
2. Anthropoid — found in North America in an approximate frequency of 20% or more; (so called because of resemblance to the pelvis of the higher ape).

3. Android—found in North America in an approximate frequency of 25%; (the female pelvis with masculine characteristics).
4. Platypelloid — found in North America in an approximate frequency of 2%; (the flat pelvis—original anthropological term: platypellic).

The frequency given in the four groups above, is an inclusive one, and takes into consideration the so-called *pure or parent types together with the pelvic forms where the parent type predominates* in the physical characteristics observed. Whereas there are stated to be four parent forms there are also 14 possible mixed forms, recognizable for all practical purposes. The proportion of pure or parent forms, together with that of the mixed forms, varies in various parts of the world as could be expected from pre-existing anthropological studies. The denomination of the mixed types is made by labelling each with the *shape of the posterior pelvis* as described for the parent type, with that of the *fore-pelvis* modifying the mixed type—e.g. Gynecoid-android.

In order to classify female pelves into parent or mixed morphological types it is necessary to direct our attention to:

(a) The observation of the shape of the female body as a whole, (discussed below).

(b) Analysis of the various component physical characteristics of each pelvis studied: (from manual, instrumental or X-ray study).

1. Inlet shape—(fore and posterior pelvis; determined by examination of the shape of the space anterior or posterior to the transverse diameter of the pelvic inlet.
2. The degree of sacral inclination, forward or backward, and curvature of the sacrum vertically and horizontally.
3. Symphysis Pubis — inclination, depth and thickness.
4. Side walls of the pelvis—straight, convergent or divergent.
5. Subpubic arch—with and shape of the arch; usually there exists a close correlation between the size of the subpubic arch and the degree of straightness, convergence or divergency of the side wall; but this is not necessary so.
6. Sacrosciatic notch and aperture; the latter depends for its size upon sacral inclination.
7. Shape of pelvic outlet—(fore and posterior pelvis).
8. Prominence of ischial spines.
9. Bone structure—(light or heavy).
10. Pelvic depth—(deeper in android).
11. General size of pelvis.

Review of the physical characteristics of the four parent types of the Caldwell and Moloy classification:

1. GYNECOID. *Body build*:

Narrow shoulders, wide hips, inner aspect of thighs usually separated. Well formed legs; the classical feminine body build, with light bony architecture.

Pelvis:

Inlet rounded, or a broad transverse oval; both the fore and posterior pelvis are well curved, i.e., a useful posterior pelvis. Widest transverse diameter well in advance of the sacral promontory. Side walls straight or slightly divergent, preserving the transverse capacity down to the

level of the ischial spines. The ischial spines are not prominent. Subpubic arch is moderately wide, the so-called "Norman arch" shape. Wide sacrosciatic aperture and average notch. Sacrum slopes backward and is well curved, giving ample posterior-pelvic space. Light bony structure.

2. ANTHROPOID. *Body build*:

Usually tall, with wide shoulders and narrow hips. Thighs straight: not in contact; not heavy build; legs are usually well formed. The typical tall female athletic figure.

Pelvis:

Inlet is an anteroposterior oval, though the angle of the fore pelvis may be narrow or average. Widest transverse diameter of the inlet considerably in front of the sacral promontory. Side wall usually straight or divergent; the "blunderbuss" type being occasionally found. Ischial spines not usually prominent. subpubic arch well shaped though usually narrower than gynecoid. Wide sacrosciatic notch—average aperture. Sacrum is usually long and narrow and may have six segments. Frequently inclined well backward, with a good curvature giving good space in the posterior pelvis at all levels. Bony structure lighter than the android, but heavier than the gynecoid.

3. ANDROID. *Body build*:

Usually heavy, stocky, but not necessarily fat (as any of the morphological types may be found in fat women). Typical body build is masculine in form, with thick, straight thighs and legs, usually in contact.

Pelvis:

Wedge or blunt heart shaped inlet, with narrow fore-pelvic angle. Side walls convergent. Widest transverse diameter close to sacrum giving a poor posterior pelvis—which may exist at all levels. Sacrum usually inclined forward in the posterior pelvis, approaching the ischial spines, to produce a narrow sacrosciatic notch and aperture. Narrow subpubic arch: "Gothic" type. Deeper pelvic cavity than the gynecoid or anthropoid type. Heavy bony structure. The pelvis may be *very male* in type.

4. PLATYPELLOID. *Body build*:

Smaller gynecoid type with the same general bony characteristics: i.e., usually a light build.

Pelvis:

Simply a flattened gynecoid pelvis. Transverse oval inlet, with widest transverse diameter midway between the sacrum and symphysis pubis. Posterior pelvis at all levels tends to be gynecoid in type. Subpubic arch, sacrosciatic notch, sacral position and curvature, generally gynecoid in form. Pelvic side walls usually straight, though pelvic capacity is limited due to the anteroposterior flattening. Light bony architecture.

IN REVIEW: In the practical consideration of pelvic morphology in relation to the possible mechanism of labor our attention must be directed to:

1. Observation of body form and inclination of the pelvis in the erect position.

2. Analysis of the various components of the pelvis making up the morphological type, by manual, instrumental, or radiological methods.
3. Morphological study of the foetal head: dependent on improved radiological technique, and possibly the use of the precision sterescope (designed by Caldwell and Moloy).
4. The mode of adaptation of the foetal head, considering its shape as well as its size, to the pelvis at various levels.
5. The extent of mouldability of the foetal head, so necessary to overcome certain degrees of disproportion due to size and shape of pelvic inlet, cavity and outlet.
6. The possibility of pelvic adaptability to the foetal head; resulting from increased pelvic joint mobility in pregnancy, actual joint widening; variation in pelvic inclination; and sacral rotation backward during the second stage of labor. This latter factor should and can be utilized during delivery when there exists a narrowing of mid-pelvic diameters, especially the sacro-pubic and bi-spinous.

The factors controlling the duration or difficulty in labor, *in addition*, depend on:

(a) Strength and frequency of uterine contractions: powerful and frequent labor pains obviously will overcome higher degrees of disproportion, than poor infrequent pains. The efficiency of the mechanical effort of the uterus in labor cannot be measured quantitatively.

(b) Character of the soft tissues; degree of rigidity, elasticity, etc.

(c) Physical condition of the patient in labor.

It is important to avoid placing too much confidence in *pelvic measurements alone* whether obtained manually, instrumentally or by X-ray. Even simple manual impressions, e.g., as to diminished lower pelvic and outlet capacity, may be quite misleading when we see uterine force in action in opposition to foetal-pelvic adaptability. Foetal cephalic and maternal pelvic morphological adaptation may be equally as important as the apparent adequacy of pelvic diametric measurements. Particular care should be taken before and in early labor to determine, gently the *available* space in the fore or posterior pelvis, especially at the midpelvic level and at the outlet. N.B.: a *rectal digital approach* to the assessment of the midpelvis and outlet is most useful, eliminating the often confusing resistance of an inelastic vaginal outlet and perineum. This is best accomplished with the patient in an exaggerated lithotomy position, i.e., having the patient pull her knees close to her abdominal wall. It is a quite simple method, and can be used on your own office examining table.

PROBABLE MECHANISMS OF LABOR *in relation to the main pelvic Morphological types:* The four subdivisions below include not only the more or less pure types, but *also the mixed forms* where the purer morphological type elements predominate, e.g., Gynecoid and the gynecoid mixed forms. The following is a review based to a large extent upon the observations of Caldwell and Moloy:

1. GYNECOID, and gynecoid mixed types: Engagement of the long axis of the foetal head is usually in the maternal pelvic transverse diameter in approximately 54%; and anteriorly in the oblique diameter in approxi-

mately 16% making a total of about 70%. The remainder engage as occipito-posteriors. 75-90% of these will rotate spontaneously at the mid-pelvic level, due to adequate mid-pelvic space. One may state dogmatically that there is usually no significant outlet problem which cannot be dealt with by the careful use of obstetrical forceps plus a deep episiotomy if necessary.

2. ANTHROPOID, and anthropoid mixed types:

The majority engage as direct occipito-posteriors, or direct occipito-anteriors; though, *due to the proportion of anthropoid mixed types found*, as high as 35% may engage in the transverse diameter, or in the anterior oblique diameter. The direct occipito-posterior position is decidedly characteristic of this pelvic type; and delivery as such is not uncommonly spontaneous. If transverse arrest or occipito-posterior arrest of the foetal head occurs at mid-pelvic level, either may be rotated at a low level, as long as the posterior pelvic space is adequate. Outlet difficulty is uncommon due to the backward inclination of the sacrum.

3. ANDROID, and android mixed types:

Engagement in the transverse diameter is almost three times as common as both the occipito-anterior and posterior positions combined. There exists a definite predisposition to occipito-posterior and transverse arrest at the mid-pelvic level. Here, the transverse arrest is usually the original position maintained from the higher pelvic inlet level. Rotation is best conducted at the upper mid-pelvic level, due to the usual lack of posterior-pelvic space at a lower level. Outlet and lower pelvic problems are most marked in the android type, due to the poor posterior pelvis which may be found. This likelihood can be forecast as a rule by prenatal pelvic rectal examination; though the possibility of mid-pelvic and outlet disproportion should be checked again rectally in the exaggerated lithotomy position *at the onset of labor*, when one also can assess the *probable* adaptability of the foetal head, and its relationship to the mid-pelvis and outlet. If the sacrum is straight and inclined forward, with a narrow subpubic arch, serious mid-pelvic disproportion is predictable unless the child is small or morphologically adaptable. Assessment of the lower posterior-pelvic space improves with experience and it is important as stated, that such be rechecked early in labor: especially if a large child has, with some delay, become engaged. Caesarian section may be indicated at term, prior to onset of labor in a *small* number of cases after careful evaluation; though *absolute* disproportion due to the convergence of the lower pelvis is rarely found. Lower pelvic and outlet disproportion is uncommon if the foetal head descends to the level of the ischial spines without an undue prolongation of labor. However, *sufficient degrees of lower mid-pelvic and outlet disproportion* may lead, as one knows, to:

(a) Difficult outlet delivery with intra-cranial injury to the child, stillbirth, or neonatal death;

(b) Severe maternal soft tissue injury, including damage to the urethra, bladder and rectum;
(c) Fracture of sacrum, or separation of the symphysis pubis.

In the android type of pelvis especially, one should pay particular attention to the prominence of the ischial spines, which narrow the available bi-spinous diameter of the mid-pelvis; as an apparently adequate bi-tuberous (transverse diameter at the outlet) diameter may exist in conjunction with a narrow bi-spinous diameter. Furthermore, the posterior-saggital diameter at the outlet is almost invariably somewhat greater than that at the mid-pelvic level. One may utilize more efficiently, posterior pelvic space at the mid-pelvic level and outlet, in the following way (as pointed out by Hanson: "Sagittal Expansion in Narrow Midpelves," American Journal of Obstetrics & Gynecology, Vol. 63, p. 1312-17, June 1952). The exaggerated Sims position in second stage labor is recommended to permit sacral rotation backward, before actual delivery. Also an exaggerated axis traction forceps delivery is valuable—with a thick soft rubber pad under the buttocks to allow sacral rotation. The assistant exerts moderate downward pressure on the handles of the forceps, close to the perineum, at the same time the obstetrician intermittently applies traction in the usual manner with axis traction forceps. A deep mediolateral episiotomy is advised.

4. PLATYPELLOID, and platypelloid mixed types:

Usual engagement is in the transverse diameter as stated; and transverse arrest is not uncommon, due to the diminished fore-pelvic capacity in this type of pelvis. However, to repeat, there is usually sufficient posterior pelvic capacity within the mid-pelvis to undertake rotation at that level.

N.B. In the rotation of any transversely arrested head in the mid-pelvis depending on the relative amount of space in the fore-pelvis or the posterior pelvis, the head should be laterally flexed into the greater of the spaces before rotation is attempted. This is both a practical and useful suggestion made by Caldwell and Moloy.

CONCLUSION. The most valuable measurement of pelvis morphology and capacity is the foetal yardstick. In case of cephalic disproportion at the level of the inlet: if, during a test of labor, the presenting part cannot traverse this superior strait, the capacity of the pelvis below that level becomes a matter of mere academic interest. If by manual pressure on the uterine fundus, the presenting part at full term can be pushed to the level of the spines *before the onset* of labor, or descends during labor to this level with no undue delay, the probability of serious mid-pelvic and outlet disproportion is slight. As stated above, marked outlet disproportion, in the absence of mid-pelvic disproportion, is rarely found.

THE ORIGIN AND SPREAD OF CANCER

JOHN D. HAMILTON, M.D.*

Introduction

In the latter part of the 19th century, Cohnheim postulated the theory that cancer arose from embryonal cell rests. Although this theory lost favour a good many years ago, some of its implications have persisted until the present day. For example, the belief is still commonly held that cancer arises from a single cell or a single group of cells, without any preceding change or accompanying change in the immediately adjacent tissue, and that *such a cancer in its earliest stages is confined to a very small area*. It is my purpose to-day, to try to convince you that the focal point of origin is fallacious, with regard to malignant epithelial tumors.

If we discard Cohnheim's theory of embryonal cell rests as the cause of cancer, and accept the current theory that most epithelial cancers arise through the prolonged action of some irritant on the cells, it is obvious that the unknown irritant, whether it is chemical, or physical in nature, will not act on an isolated cell, but on an area of identical cells. If we take sunlight as an example of a cancer promoting agent, all the exposed surfaces of epidermis will be affected, albeit all areas not equally so. For many years, the injurious effect of actinic rays may not produce any gross or histologic change in the skin. In most individuals it never does, but in those of fair complexion and probably of inherent susceptibility as well, there ultimately appears the senile keratosis. This may be single or multiple, appearing at different times over a period of years. The gross appearance of these lesions is that of a circumscribed thickening of skin, usually with a white, and scaly surface. The histologic picture is one of an increased thickness of all layers of the epidermis due to abnormal proliferation of normal appearing cells. The rete pegs are larger and thicker, one sees frequent mitotic figures, and a greatly increased layer of keratin. The keratosis is a localised area of hyperplasia and results from the action of an irritant which stimulates the cells to excessive growth. We know that the surrounding normal appearing epidermis is not normal, because at any time another area of hyperplasia, and another keratosis, may appear. In other words, an area of skin has been altered by the actinic rays, and probably by age and susceptibility as well, so that it may erupt into abnormal activity at any time at one or more points. A further progression of the lesion is the development of epidermoid cancer in one or more senile keratoses. The exact point at which a benign keratosis becomes malignant is very difficult to define, not only grossly but also histologically. It is quite generally accepted by those actively engaged in surgical pathology that lesions are encountered in which one cannot tell with certainty whether that subtle change from hyperplasia to malignancy has or has not taken place. When malignant change does occur, we find that it does

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not develop in one group of cells in the keratosis, but may arise in several of the hyperplastic areas of the lesion at the same time. Furthermore as the malignant change spreads, we see the surrounding epithelium showing first hyperplasia, and then a transformation into the disorderly growth characteristic of neoplasia. There is a gradual change from normal appearing epithelium to hyperplasia, to malignancy. This form of epidermoid carcinoma then develops in one or more areas of skin prepared by a cancer promoting agent. It has a field of origin, and is mediated through an excessive but normal appearing overgrowth of cells.

The natural history of skin cancer has been verified experimentally through the work of Peyton Rous and his associates. They showed that the application of tar to the skin of mice over a period of many weeks gradually produces a hyperplasia which ultimately becomes malignant, but again the point at which the malignant change supervenes cannot be definitely determined. They also demonstrated that a subtle change takes place in cells through the action of the cancer promoting substance so that after a time non-specific irritants, such as hot water or wound healing may be the trigger mechanism by means of which cells lose their orderly manner of growth and become disorderly and malignant.

These observations mean from the practical standpoint, that the individual who develops an epidermoid carcinoma on the dorsum of his hand and has it removed, may subsequently develop more cancers, which have arisen not because of incomplete removal of the original keratosis or early cancer, but because all the cells of the back of the hand have been acted upon by a cancer promoting agent. The rate at which cancer develops in that area of skin will, however, vary from one point to another. I know that surgeons have long believed and rightly so, that all cancers no matter how small should be widely excised. Their reasons, however, for such wide excision I believe are based upon their fears of spread, their fear that the cancer has extended into subjacent lymphatics. What they are not so aware of is that all of the tissue sometimes for several centimeters around, may be in a precancerous state, albeit there is no gross evidence and usually no histologic evidence of such a transformation.

Although the field of origin of epithelial cancer has been most ably demonstrated in the skin, it has also been demonstrated in mucosa of mouth and genital tract, and in the breast, in certain types of chronic mastitis, through the work of Dawson, Cheatle and Cutler and others. More recently Gall, at the University of Cincinnati, by making sections of whole organs has demonstrated that cancer of the gastro-intestinal tract, most notably stomach, and colon, may also have a field of origin with two or more growths arising over a fairly wide area of mucosa. Here too, however, the rate of malignant transformation within the mucosa varies greatly, and one may find an easily recognizable gross lesion and at several centimeters distant a small very early lesion arising in the more superficial parts of the mucous membrane. By means of these organ sections Gall was able to exclude metastatic spread as an explanation of the multiple origin of cancer of the stomach and colon.

Spread of Cancer. You are all aware of the commoner means of spread of

cancer which is by direct extension, by invasion of lymphatics and by invasion of blood vessels. There are, however, a few facts about the spread which I believe are of practical importance. The ability of a malignant epithelial tumor to spread depends upon certain cellular characteristics. These include its exaggerated rate of multiplication and growth, the ability of individual cells to move by ameboid motion, and the fact that cancer cells do not adhere to one another the way normal cells do. Cancer cells tend to dissociate. This latter fact is widely made use of, in the study of various bodily fluids for cancer cells, for example, vaginal and bronchial secretion. Granted then that cancer cells have this motility, their spread will be determined in large part by their rate of growth. We recognize, however, that all cancers do not grow at the same rate. Those which are histologically highly anaplastic and embryonal in appearance we know will spread rapidly and metastasize widely throughout the body. This I believe is directly related to the greater lack of cohesion and greater power of ameboid motion of the individual cells. We encounter every gradation between these rapidly metastasizing growths and those which remain localized to their area of origin for indefinite periods. Generally speaking, the more that cancer cells resemble normal cells the less their rate of growth. The more differentiated the cell is the more cohesive and the slower its rate of multiplication. One does see, however, tumours which appear histologically malignant but not too anaplastic, which generally do not spread and it is about some of these tumors that I wish to speak. One is the X-ray carcinoma, by which I mean, an epidermoid cancer which develops in an area of X-ray dermatitis. This is not an uncommon lesion to encounter today, principally because of excessive radiation therapy given some twenty years ago. These tumors arise usually in a densely scarred area where the epidermis may be thin and atrophic in appearance and the underlying dermis and subcutaneous tissue dense, hard and contracted. Surgeons recognize, and have for many years, that X-ray cancers don't readily metastasize. Similarly, epidermoid cancers arising in old wounds such as varicose ulcers do not spread rapidly. Here again the epidermis is thin and atrophic and the underlying tissue densely fibrotic. It is my contention and that of Willis, that these cancers do not spread because they are unable to penetrate the dense scar tissue. Scar tissue is exceedingly poor in capillaries and lymphatics. The tissue spaces are practically non-existant because of the dense collagen bundles which fuse and become hyaline. The chance for cells to wander through such a tissue are exceedingly poor because cancer cells are fragile things and will only move along unobstructed pathways where they are bathed in tissue fluids. There recently appeared in one of the reports of the Staff meetings of the Mayo Clinic, a case of carcinoma of the breast in which there had been numerous recurrences in the scar of the radical mastectomy, these recurrences appearing over a period of some nine years. Here again I believe, the recurrences had been localized without generalized dissemination simply because the cancer cells were unable to penetrate the dense barrier presented by the scar tissue.

There is a further example, illustrating another point in the carcinoid tumor of the appendix. You are probably all familiar with them, they are occasionally

encountered at operation and at post mortem. They are small, firm tumors, usually in the tip of the scarred appendix, and are composed of large, clear, epithelial-like cells. These cells grow in nests and penetrate all parts of the appendicial walls. In the appendix, however, they remain localized and there are no recorded cases of dissemination from the appendix to other parts of the body. When we encounter this same tumor in the ileum, the story is quite different, because carcinoid tumors of the ileum do metastasize to the liver and sometimes throughout the body by way of the blood stream. Why then is there this totally different behaviour of histologically identical tumors? They both take origin from the argentaffine cells. The only explanation which is logical is that the local conditions in the two organs are not the same. In the appendix the tumors are found in old scarred tissue, where there is no movement. The appendix remains as a quiescent organ in such cases, the muscle having been destroyed by the preceding inflammation, which produced the scarring. In the ileum, on the other hand, there is intermittent contraction and relaxation of the musculature. Lauzé postulates that it is this continual movement which squeezes the cells into the lymphatics, and when they get into the lymphatics they are carried, possibly by the lymph flow, possibly by direct growth, to the abdominal lymphatics. Similarly, these cells may be squeezed into capillaries and eventually reach the liver. This latter example illustrates quite well I believe, the importance of motility of an organ in the dissemination of cancer into the blood stream and into the lymphatics. In those tissues and organs where there is little or no movement, the cancer may not spread until relatively late in the course of the disease. Other factors of course which must be taken into consideration are the degree of differentiation of the tumor, its rate of growth, the ability of its cells to dissociate and wander into tissue spaces, multiply rapidly, and thus gain entrance into lymphatics and blood vessels. It is, I believe, the contraction and expansion of organs such as the stomach and lung which are largely responsible for the early dissemination of cancers of these organs, and therefore responsible for our exceedingly low survival rates in any form of treatment we know today.

In summary, then, I have tried to point out that epithelial cancers in particular have a field of origin and that recurrent cancer may not be recurrent in the sense that the original cancer was not entirely removed but may be the development of a new cancer in an area of tissue which had suffered through the action of the same cancer promoting agent, albeit the rates of malignant transformation may differ widely in different areas. The second fact I have tried to stress is that of movement of organs and tissues being in considerable part responsible for the dissemination of cancer through lymphatics and blood vessels to other parts of the body.

For one mistake made for not knowing, ten mistakes are made for not looking.

J. A. LINDSAY

MEDICAL AND MILITARY ASPECTS OF FASTING

J. Q. BLISS, B.A., 5T6

FASTING, in a religious sense, may mean any number of things; but in medical and military terminology it means simply "going without food". The term does not imply abstinence from water.

I

Medical interest in fasting is largely two-fold: (*a*) fasting is a useful experimental tool, and (*b*) the fasting subject provides an interesting study in metabolic adaptations to an abrupt change in the body's energy sources.

A. EXPERIMENTAL USES

Fasting is often used as an experimental method for producing various effects.

Fasting can be employed to induce a moderate degree of ketosis in man and in monkeys. Dogs, rats, and other animals are less susceptible (1).

A less obvious use of fasting is in the production of a reversible decreased glucose tolerance (2), as discussed presently.

Fasting can be used to decrease the insulin content of the pancreas (3), especially in rats, and has many more complex applications in the study of metabolic and endocrine relationships. It is particularly useful as a means of subjecting an animal to stress.

B. THE METABOLISM IN FASTING

During a fast the body must rely solely upon its endogenous resources for the maintenance of its energy metabolism and electrolyte balance. Many aspects of its metabolism are accordingly altered.

CARBOHYDRATE METABOLISM

During the first few hours of a fast, the body derives its energy from its glycogen stores. These are rapidly depleted, however, and after the first day of a fast the body derives nearly all its energy from fat and labile protein stores.

An important feature of this derivation of energy from fat and protein rather than from carbohydrate is that it decreases the ability of the body to utilize exogenous carbohydrate. Thus if glucose is given to a subject who has fasted several days, a "diabetic" response ensues. The blood sugar level shows a prolonged rise, glucosuria occurs, and the respiratory quotient does not show the normal rise which is expected after glucose administration (2). This defect in carbohydrate utilization during fasting was discovered in 1889 by Hofmeister, who called it "hunger diabetes" (4). Its mechanism of production is not entirely clear, and has been variously attributed to a depression of insulin liberation, a decreased sensitivity to insulin, or an alteration in enzyme activity (5).

Although glycogen stores are reduced very early in fasting, they are not completely exhausted. At the same time, a normal or near-normal blood sugar level is maintained during long periods of fasting. For this maintenance of glycogen reserves and the blood sugar level, protein and/or fat must be converted to carbohydrate. This conversion undoubtedly occurs in the case of protein, although the metabolic pathways have

been elucidated for only a few of the amino acids (6). Evidence for the conversion of fat to carbohydrate is indirect and somewhat controversial (7).

PROTEIN METABOLISM

Urinary nitrogen excretion may be taken as a close measure of protein catabolism during a fast. During the first day of a fast after a mixed diet, when the body is subsisting on its carbohydrate reserves, nitrogen excretion drops sharply (8, 9). A rise in nitrogen excretion ensues as the body draws upon protein for energy. In humans, the rise reaches a maximum of 15-20 g. per day in two to four days and then declines to about 5 g. per day (9, 10). This decline can be attributed to (*a*) a depletion of labile body protein stores, causing a decrease in the derivation of energy from protein (11), and (*b*) a decreased metabolic rate, the regular observation in fasting (12).

FAT METABOLISM

The fasting subject is soon called upon to obtain almost all his energy from his fat stores. An enormous increase in fat catabolism occurs, and this results in the most prominent metabolic feature of fasting, ketosis.

Ketosis is the occurrence in the body of abnormally high amounts of aceto-acetic and beta-hydroxybutyric acids, and their breakdown product, acetone. These three substances are known as the "ketone bodies". Under normal dietary conditions, the blood ketone body level in humans is 3-5 mg. %, but in fasting this level climbs to 50-100 mg. % within three days (10). Urinary ketone body excretion is low the first day of a fast, but rises to 4-8 g. per day by the third day, and remains at this level for the duration of the fast (10). Thus ketonuria is always associated with fasting in humans.

There is general agreement that the site of origin of acetoacetic and beta-hydroxybutyric acids is the liver (13). It is also generally agreed that these acids represent intermediaries of fat catabolism, and that the peripheral tissues can utilize them in large amounts for energy. Indeed, more than half the energy required by the fasting animal may come from the catabolism of the ketone bodies to carbon dioxide and water (13).

A remarkable aspect of fasting ketosis is that a very small amount of exogenous carbohydrate can completely eliminate ketone body accumulation. As little as 50 g. of glucose daily will prevent ketosis in the otherwise fasting human (14). Investigators disagree as to the exact mechanism whereby carbohydrate exerts this anti-ketotic action. Thus Soskin (15), Stadie (13), and others think that carbohydrate acts in the liver to decrease ketone body formation by counteracting the predominance of fat over carbohydrate in the competition for available oxygen or enzyme systems. Breusch and others (16, 17), however, have presented evidence that the ketone bodies are catabolized through Krebs' cycle, and that carbohydrate may act by "speeding up" the cycle in the peripheral tissues. The evidence at present is too conflicting for a definite conclusion.

MINERAL METABOLISM

The fasting human takes in no salts, yet, unless the heat load is high, he suffers no serious upset of electrolyte balance. This is surprising in view of the fact that the fasting subject is continually being called upon to excrete unusually large amounts of organic acids as a

result of his ketosis. How does the body provide base for the excretion of these acids, and at the same time maintain its electrolyte balance? Several mechanisms operate (18, 19):

1. During the first few days of the fast, considerable amounts of sodium are provided for combination with acids through a decrease in extracellular fluid volume.
2. Potassium is made available for excretion with acid from protoplasm broken down for energy—i.e. intracellular fluid is decreased, with a release of potassium.
3. Calcium is released from osseous sources for excretion with acid.
4. Most important is the formation in the kidney of ammonium ion (from urea) which replaces to a large degree sodium and potassium cations in the excretion of acid.

It should be noted also that base is conserved through the kidney's ability to excrete a urine with a more acid reaction than the plasma. Thus some acid is excreted uncombined with base. This accounts for the marked acidity of the urine during starvation.

II

The layman is often surprised to learn that fasting is a matter of interest to the armed forces. It is true that frank starvation seldom if ever occurs among modern armies, since when food runs short the soldier generally subsists at the expense of the civilian. In one military situation, however, total starvation often assumes a disturbing prominence. This is the "survival situation".

The term "survival situation" refers to the situation in which an individual (or a group of individuals) is abruptly and without warning isolated from his unit in such a fashion that re-contact with his fellows may be delayed for days, weeks, or indefinitely. The airman who bails out in the Arctic, the infantryman who gets lost in the jungle, or the seaman who abandons ship in mid-ocean—all are in typical survival situations.

It is apparent that in many of these circumstances the individual is unable to obtain food from his environment, so that, unless he has brought rations with him, he is faced with the prospect of a total fast of indefinite duration.

In order to obtain proper perspective, is should be stated at the outset that starvation is usually not the most important aspect of the survival situation. In the desert, a man can die in less than 48 hours if without water and unprotected from the heat. In the Arctic, death from exposure can occur no matter how adequate the food supply. Even in situations where the environment is favourable, fear often impairs a man's ability to survive more than does starvation. Accordingly, the man confronted with a survival situation must be equipped primarily to survive his environment and his own mental deterioration. Starvation per se is not the immediate problem.

This reservation does not lessen the importance of starvation as an adverse factor in survival, however, because, as will be shown, the problems of protection from environment and maintenance of mental stability are intimately related to the problem of starvation. With this in mind, let us consider the effects of fasting upon the isolated individual, and what can be done to cope with them.

In a survival situation, the most important effect of fasting is probably psychological. Even the prospect of starvation can cause so much fear in some men

that their judgment is seriously impaired. After a day or two of fasting, fear is accentuated, and even those men who do not experience fear still suffer a decline in morale. Although poor morale might be expected in any case in a survival situation, fasting alone can cause a poor mental outlook. Men used as subjects in fasting experiments show marked irritability and depression even though they know a good meal is assured in a few days (9).

What can be done to deal with this problem? One obvious remedy is to equip aircraft and ships with rations specifically designed and designated for survival purposes. This is now done almost universally. Even jet-aircraft, which have extreme space limitations, are equipped with emergency rations. In this way, the isolated serviceman need not face the prospect of total starvation right from the start of his survival experience.

A further and invaluable aid to the survivor is proper training before he is subjected to survival conditions. The serviceman can be taught that no serious consequences will be suffered from two or three weeks of starvation, and he can be taught that "living off the land" is possible even in the Arctic. Actual "survival schools" for this training now exist both in Canada and the United States. As an airman who actually underwent a survival experience in the South Pacific puts it: "No amount of survival equipment will help some men, while others, through sheer ingenuity and determination and under similar circumstances, will fare much better and return regardless of whether they possessed equipment or not. It's largely a mental outlook . . . the will to survive is the deciding factor." (20).

Aside from its effect on morale, fasting alone does not produce striking disability for several weeks. Although a fasting man complains of weakness and is usually incapable of prolonged exertion, he is by no means "bed-ridden". Several officers of the R.C.A.F. who fasted for ten days last summer managed to drive a car 175 miles on the 6th day of their fast, and repeated the performance on the 7th day. One of these men ended his ten day fast with a small meal of bacon and eggs, and then swam one mile unaided! (21).

This should not imply that a small daily ration does not improve one's chances of survival, however. It has already been mentioned that a small ration is better than none from a psychological stand-point, and this is also true from a physiological stand-point. As stated previously, 50 g. of glucose daily is usually sufficient to prevent ketosis. 100 to 200 g. of glucose daily also conserves up to 50% of body protein otherwise broken down for energy (9, 14). These effects of glucose are of utmost significance to the man whose water intake is severely restricted, because (*a*) prevention of ketosis means prevention of the dehydration associated with it, and (*b*) a conservation of body protein means a reduction in urinary nitrogen excretion, and hence a reduction in body water lost in the urine. The water of oxidation of glucose is of further help to the body in water restriction. Taking all these factors into account, it has been estimated that 100 g. of glucose will conserve about 250 g. of water (14). Thus we see that a few hundred Calories of carbohydrate can be of great value in surviving adverse environmental conditions.

So far, glucose has been mentioned as

the survival ration, and, where space limits the size of the ration to 400-800 Calories per day, it appears that a high proportion of carbohydrate in the ration is indeed desirable. It is true that fat has a much higher caloric density than carbohydrate, but a ration containing a high proportion of fat is of little value in preventing ketosis, and may actually accentuate it. A high proportion of protein in the ration has the serious disadvantage of increasing the urinary nitrogen excretion, thereby increasing the loss of body water.

This is not to say that the survival ration should be composed entirely of carbohydrate, however, for investigations by Schwimmer in the U.S. (22, 23) suggest that, at the 900 Calorie level, the incorporation of moderate amounts of protein of high biological value (egg albumin) actually decreases the nitrogen excretion. That is, this protein is used by the body to build or maintain tissue proteins. Schwimmer's results suggest in addition that some fat in the ration also may be effective in promoting nitrogen retention.

In conclusion, it may be stated that, at low caloric intake levels, the optimum proportions of carbohydrate, protein and fat have not been determined exactly, but a high percentage of carbohydrate, with smaller percentages of protein and fat, appears to be satisfactory in terms of water balance, nitrogen balance, and anti-ketotic activity.

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The Lord may forgive us our sins, but the nervous system never does.

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EDITORIAL

INCREASED STIPEND

Final year students anxiously contemplating internships are more than casually interested in a recent announcement from the teaching hospitals of another large Canadian medical centre. Applicants for junior internships in these hospitals have been notified that the new honorarium, previously non-existent, has now reached the sum of three hundred dollars per year or three times the amount paid by corresponding local hospitals.

Teaching hospitals in the past have been adamant in their stand toward interne remuneration, pointing out: (*a*) the real value of an interne to the hospital is questionable, and (*b*) the knowledge and prestige the interne will obtain should be ample reward for his services.

These arguments are very true and worthy of repetition, but if the present graduating year is any criterion, they are views which are not fully appreciated by the average medical student.

Increased remuneration will never be a measure of advancement in medical science. However when reasonable increases are made, it indicates a desire by the hospital concerned to obtain a wider selection of applicants by considering more needy students who would otherwise be lured elsewhere.

At the risk of sacrificing altruistic ideals, perhaps this plan is the solution to the teaching hospitals' ambition lately unfulfilled—that of having unlimited suitable applications for the junior internships they offer annually.

ALLERGY IN RELATION TO SKIN DISEASE*

P. URBACK, 5T3

I THINK it was Sir Clifford Albutt who said that of all things in medicine, definitions are the hardest—probably because they are so crucial. The statement is particularly applicable to tonight's topic.

There are some interesting tendencies in current medical thought with regard to allergy. There is a group which seems to equate the term with anything strange or mysterious and even to use it as a synonym for idiopathic. At the other extreme, there are some people who frown upon calling anything allergic, preferring to use such euphemisms as hypersensitivity, immunity, etc. Both attitudes are in my opinion equally deplorable.

ALLERGY

The term was introduced by Von Pirquet in 1906 to designate "any acquired specific alteration in capacity to react of living tissue upon exposure to certain foreign agents". The important points are

1. Change is a *qualitative* one—not merely a statistical change in degree from the normal reaction but a change in type, a new kind of reaction.

2. It is *specific* and extremely so; it is manifest only on re-exposure to the same or to an immunologically related agent.

3. It is *acquired*. No tissue is a priori allergic. An environmental factor is always necessary.

*From a paper delivered to the A.O.A. Society, Jan. 12, 1953.

WHAT ALLERGY IS NOT

1. *Hypersensitivity* — allergy is not necessarily hypersensitivity.

(*a*) A man is not necessarily hypersensitive to tuberculin when he is in reality relatively immune (cf. BCG vaccination).

(*b*) A man who reacts to 1/20 mg. OT is allergic and sensitive.

A man who reacts to 1 mcg. OT is allergic, sensitive, and hypersensitive.

(*c*) The specific alteration in the capacity to react may be in the direction of increased or decreased sensitivity. E.g. skin does not react on re-exposure to tetanus toxin.

2. *Immunity.*

It is not sensible to call a guinea pig immunized to a substance when the poor animal is so the opposite of immune that exposure to a single drop of 1:1,000,000 diln. of agent concerned can suffice to bring about his rapid demise.

CHARACTERISTICS OF ALLERGIC RESPONSE

The principles can be derived from a simple experiment done by Sulzburger on human volunteers. A drop of a suitable dilution of a synthetic chemical (1-2-4 dinitrophenol) was put on the skin and the reaction was observed.

1. In a certain number of cases nothing happened. They were refractory to the allergen.

2. A large number had a reaction (erythema and vesiculation) at the test site after 4-20 days, i.e. there was an in-

cubation period and a spontaneous flare-up. During the incubation period, the sensitivity of the tissues gradually increased until it was high enough to react with what antigen remained at inoculation site, and a flare-up resulted.

3. Re-application of the chemical to their skin now manifested an altered capacity of the tissues to react. The incubation period vanished. There was a latent period of 24-48 hrs. (cf. days previously) before the reaction occurred. This is obviously a different mechanism and is not well understood. It is constant of different allergies and may be early (5-30 min.) as in urticaria or delayed (24-48 hrs.) as in contact dermatitis.

Summary

1. Refractory period on 1st exposure.
2. Incubation period.
3. Spontaneous flare-up.
4. Subsequent re-exposure with loss of incubation period and accelerated reaction which may be early or delayed.

Clinical Example: Serum Reactions

1. On first exposure to horse antigen, there is an incubation period of 1-2 wks. If patient had an IC injection, he may develop a local spontaneous flare-up (local serum sickness) or if there is enough antigen in the circulation the flare-up is generalized (serum sickness).

2. On re-exposure there is a loss of the incubation period and the latent period may be early (Anaphylaxis-minutes) or delayed (accelerated serum sickness) which occurs in 2-3 days.

These principles can be clincally demonstrated most often in allergy of infection and in contact dermatitis, in many cases of drug eruptions, and in certain cases of urticaria. Of course, it is often difficult to do so in the ordinary patient.

Before continuing with general concepts of pathogenesis, I would like to examine the allergic dermatoses separately.

A. Allergy of Infection

This group is concerned with the allergic response to a *living antigen*. It is characteristic of certain infectious diseases like TB, lues, and various viral and fungus diseases. It is sometimes called the tuberculin-trichophyton group.

The *shock-organ* is all the constituents of the dermis especially the superficial blood vessels. The *allergen* is a microorganism brought to the shock-organ by the blood stream. The *characteristic pathology* is a cellular accumulation first of mononuclears and later of epithelioid cells plus evidence of vascular and connective tissue damage. Because the shock-organ is dermal, we use the *scratch or IC test*. The patch test is for epidermal sensitivity. The *latent period* before reaction is 24-48 hrs., i.e. of delayed type. The reaction is a reproduction of the characteristic pathology of the disease process (a general law for all skin tests) i.e. cellular accumulation and vascular damage. Clinically, there is erythema → induration → papule.

There are no antibodies in the serum. They are in the mononuclear cells and can be passively transferred through them (Lawrence). Eosinophilia is absent.

ID reaction

This is a characteristic manifestation of this group. I imply no Freudian overtones but rather a generalized symmetrical eruption characteristic of a hematogenous distribution which appears suddenly in a patient suffering from a focus of infection somewhere. It is a secondary manifestation of a disease

from which the patient is already suffering. It appears only in a specifically sensitised tissue (usually the skin) and is produced by micro-organisms and/or their allergenic products emanating from a remote focus.

This focus may be a tuberculous lung, a boil on the skin, a primary chancre, fungus infection between the toes, etc. The term "id" is added to the name of the primary disease. Thus we can have tuberculids, syphilids, trichophytids, and bacterids. Sometimes we find eczematids as examples of non-infectious allergy.

The pathology may be characteristic of the primary disease (e.g. tubercle in TB) or quite different. The diagnosis is made certain only by the demonstration of the primary lesion or obtaining a history of it.

In a short paper like this it is impossible to discuss individually the various tuberculoderms or syphiloderms, etc. However they all have the same basis. This basis was clearly outlined by Koch in his classic experiments on tuberculous infection in the guinea pig.

i. *Cutaneous 1st infection*

When virulent bacilli are injected IC into previously non-exposed guinea pigs, a characteristic reaction ensues.

1. There is an incubation period of 8-12 days.

2. A spontaneous flare-up occurs; inflammatory reaction → nodule → eventually ulceration.

3. Early generalization of the infection (bacilli present in blood and lymph glands in 15 min.).

4. Many micro-organisms easily demonstrable from the lesion.

5. Ulceration occurs 4 weeks after the infection. The bacilli disappear, tuberculin reaction becomes positive, and tubercles appear. This is in accordance with the *Jadassohn-Lewandowsky* law which states that whenever organisms or their products are being rapidly overcome or neutralized by the local immune-biologic processes, tubercles or tuberculoid structures tend to appear. Now it is difficult to demonstrate bacilli at the lesion.

ii. *Cutaneous reinoculation*

This is done after 4 weeks when the skin and tissues have become sensitized.

1. & 2. The incubation period is lost as is the spontaneous flare-up. Instead there is a latent period of 24-48 hrs. and an accelerated reaction.

3. Absence of early dissemination of bacilli—lesion either heals completely or tubercles appear (J-L law).

4. Difficult to demonstrate bacilli in the lesion.

5. May ulcerate in 8-24 hrs. (cf. 1-4 wks.) and healing quite advanced by 10th day (cf. many weeks).

6. Local healing at the reinoculation site is complete at a time when the 1st inoculation site would manifest maximal response.

The altered reaction after cutaneous re-inoculation is called the Koch phenomenon. It is the basic factor in tuberculosis and can be demonstrated in the other infections. It is important to note that the principles of the allergic response as shown in Sulzberger's experiment and in Serum Sickness are identical with those of the Koch phenomenon.

B. Contact Dermatitis

This is an acute or chronic superficial inflammation of the skin caused by contact with sensitizing agents. It is probably the commonest allergic disease. The *shock-organ* is the epidermis and the

allergen is brought into contact with it from without. The skin has 2 protective barriers namely the keratin and the oily sebum. Therefore most of the allergens are those which can penetrate the barrier to reach the skin e.g. keratolytics and detergents remove barrier, dyes are fixed in the keratin, plant oils like poison ivy are soluble in the sebum, and the local anaesthetics have specific affinity for epidermis. The common causes are simple chemicals used in industry or in medicine.

The *characteristic pathology* is intra-epidermal edema (spongiosis) → intra-epidermal vesicle evident clinically as a blister. The *skin test* used is the patch test (for epidermal sensitivity). A *delayed reaction* (24-48 hrs.) results and the disease is reproduced exactly. It is a true tissue sensitivity as no antibodies have been demonstrated. Eosinophilia is absent.

Clinically the lesions appear usually on the exposed surfaces 24-48 hrs. after contact with the allergen. There is moderate pruritis, erythema, and vesiculation. On scratching, oozing results and thus this is sometimes called eczematous dermatitis. The final results are papules, scaling, and infiltration. Chronic cases may go on to lichenification. The diagnosis is usually made by the history and the site of the lesions. Exact allergens are determined by patch test (never done in the acute stages).

Some cases are not allergic in nature but are due to primary irritants, i.e. substances which cause irritation in most people like strong acids and alkalis, etc. This is especially apt to be true in people with predisposing factors like dry fissured skins, or moist macerated skins, or skins which are poor alkali-neutralizers or occupations involving damage to the protective layers.

C. Dermatitis Medicamentosa

This is the term used for a drug induced skin eruption where the drug reaches the skin by the bloodstream regardless of the route of administration. It excludes contact dermatitis but includes eruptions due to absorption of a drug through the skin into the bloodstream (transepidermal penetration).

Not all untoward drug reactions are allergic e.g. As is a primary irritant and Ag exerts its effect through accumulation. Nevertheless, in the majority of classic drug eruptions due to agents not primarily irritant to the skin, allergic mechanisms play a significant part. Thus

1. Minute amounts of a drug well tolerated for wks., mos., or years may suddenly give rise to a severe eruption.
2. Once it occurs, a recurrence is likely with small amts. of the drug. This is very specific and so much so that there may be no response to an isomer of the drug.
3. Eruption is not a pharmacological action of the drug.
4. Identical lesions can arise from different drugs and one drug can cause different lesions in the same or other people.
5. Usual allergic phenomena are found i.e. refractory and incubation periods, spontaneous flare-ups, accelerated reactions, etc.

Some drugs are much worse than others. E.g. Nirvanol will produce lesion in 100%, Cascara never, arsphenamine frequently, and aspirin occasionally. The important point to remember is that *all drugs can cause eruptions* and that with the possible exception of vitamines and normal saline, no drug, unlike Caesar's wife, is above suspicion.

Pathogenesis

The drug is absorbed into the circulation and it or its split-products act as haptenes (Landsteiner) and combine with the plasma proteins. This combination is antigenic and the skin becomes sensitized to it. The important point here is that the common allergen in all diseases tends to be protean rather than protein. Antibodies are usually absent. The skin tests don't usually work. There is no characteristic pathology and the site of the shock-organ is variable.

Clinical picture—Drug eruptions are capable of mimicking any skin disease from simple pruritis to severe and fatal dermatoses (Dixon). Thus the great imitator syphilis has been replaced by the greater imitator drug eruption.

In general, the lesions are extensive and symmetrical, bright in color, very little systemic reaction, little pruritis, pain, or tenderness. They develop suddenly and disappear quickly (2 wks.) after the drug is withdrawn.

Certain drugs have a strong tendency to a particular form of response e.g. halogens give a follicular response, penicillin urticaria, phenolphthalein fixed lesions, barbiturates a morbilliform eruption. Many skin diseases are aggravated by drugs e.g. acne and furunculosis by halogens, eczema by salicylates, purpura by sulfa, fungus infections by penicillin. It is interesting to note that the antihistamines can cause drug eruptions. Except for the fact that tubercles are never found here, the drug eruptions are very similar to the allergy of infection.

Fixed lesions

This is a sharply circumscribed eruption recurring in the same or "fixed" sites on repeating the drug. Thus the reaction remains confined to and recurs in the same area or areas of the skin or mucous membrane. Moreover unlike the usual drug eruptions, it remains for wks. or mos. after the drug has been discontinued.

The lesion is usually discrete and begins with edema and erythema, becomes a dusky bluish colour and eventually heals with residual pigmentation. It is a true skin sensitivity for as has been demonstrated by Urbach the lesion can be moved around from spot to spot by transplantation of full-thickness skin grafts.

In this country the commonest cause is phenolphthalein while in Europe, it is aminopyrine, antipyrine, or phenacetin.

Prophylaxis

With the exception of atopy and fixed drug eruptions *the greater the concentration, the more intense and prolonged the exposure to a particular allergen, the higher the % of people who will become allergic to it.* This has found striking application in the use of sulfonamide mixtures as shown by Lehr.

D. Urticaria

This is an acute or chronic disease characterized by extreme pruritis and the development of erythema and wheals. Allergic mechanisms can be demonstrated only in some of the acute cases and very few of the chronic ones. The *shock organ* is the superficial blood vessels of the dermis. The *allergen* is brought there by the bloodstream and thus can be an ingestant, inhalant, or contactant (by transepidermal penetration). Usually a drug or food (seafood, strawberries, etc.) is involved. The *characteristic pathology* is vascular dilatation, edema, and eosinophil extravasation. *Skin test* used is the scratch or IC one. The *reaction* is *immediate* (5-30 min.)

and consists of a wheal. The blood shows an eosinophilia. Occasionally antibodies can be demonstrated in the sera by passive transfer.

E. Atopic Eczema

Atopy is the term suggested by Coca to describe a form of allergy characterized by a familial predisposition to develop certain diseases namely hay fever, asthma, certain dermatoses, and possibly a tendency to die rapidly upon the administration of foreign sera. Both by definition and in reality, they are strange people with a strange disease.

CLINICAL PICTURE

In infancy, childhood, and adulthood, there is a predisposition to certain characteristic dermatoses which are really part of the one disease atopic eczema.

i. *Infantile eczema*

In order to understand this disease we must remember that the infant is not just a small man. He is a different sort of small man and his reactions are different. His skin is more permeable than adult so that he is more susceptible to the effects of wool and silk. He reacts to an irritant with a vesicle (cf. bullous impetigo of infancy) where the adult would have a papule. He has the same disease as the adult but modified by difference in skin.

He is well until 3 mos. of age when he gets an erythematous plaque or a wheal on his cheeks. The infant rubs and rapidly changes it into a papulovesicular oozing eruption on cheeks and forehead leaving the eyes and mouth free. This may spread down the neck to forearms, wrists, outer legs, and finally the trunk. The characteristic lesion is the "juicy-looking" papule. The continuous oozing and scratching leads to secondary infection. As he grows older, he develops new skin sensitivities and loses some he had before. The eruption tends to disappear by the age of 2.

ii. *Childhood eczema* (Prurigo of Besnier)

Here the characteristic lesion is a papule not a vesicle. Rash begins on side of face and neck and has a special predilection for cubital and popliteal fossae, but can be anywhere. Lesion is scaly and infiltrated with lichenified plaques or there may be many small papules with excoriated tops especially over the exposed surfaces. The lesion is very irritable and he scratches all the time. In this period he may develop hay fever.

iii. *Adulthood eczema* (Neurodermatitis)

This is an extremely pruritic chronic disease with spontaneous remissions. It is either localized (lichen simplex) or widespread (generalized neurodermatitis). The primary lesion is a papule → secondary infection → weeping and crusting → lichenified plaques. It is usually localized to the flexures and the sides and back of the neck. The patient may develop asthma at this stage. He is not alone in his misery as in 50% of cases, there is a family history of this sort of thing.

The ordinary atopic doesn't usually have all these manifestations. He may have any combination. The dermatoses may occur as discrete or as continuous entities, and he may have one or none or all.

PATHOLOGY

There is nothing characteristic here. 50% show eosinophilia. The epidermal changes are all secondary and there is

some histological evidence that the wheal is the basic pathology. The *shock-organ* is the same as in urticaria and *IC test* yields an *immediate reaction* which is a wheal. Since the skin test usually reproduces the basic pathology of the disease concerned, this is further evidence for the role of the subclinical wheal in eczema. Why they don't all develop urticaria is another question. They have a predisposition to the development of atopic diseases only and are no more susceptible to other allergic dermatoses including urticaria than anyone else (Sulzberger). Prausnitz-Küstner or PK reagins or antibodies are frequently found in their sera. These are skin-sensitizing antibodies which can be demonstrated by passive transfer. They are characteristic but not pathognomonic of atopy.

ETIOLOGY

It is difficult to be very definite here as there is such a hodgepodge of allergic, psychogenic, and various irritant factors involved. The skin test doesn't help us much because these patients will react to almost any potential allergen with which they come into contact. We know that almost any skin disease can be profoundly affected by psychological factors but these seem to have especial importance here. Moreover their skins seem to develop a true hypersensitivity so that they will react severely to substances like wool and silk which are only mild primary irritants in most people.

In infancy foods are very important at least to the end of the 1st year. The infant can become allergic to almost anything in the diet including milk, eggs, pablum, orange juice, and cod liver oil. The inhalants are far more important here than is usually realized. Contactants such as the mother's dandruff, dirt, soap and water, etc., often aggravate the condition.

In childhood, foods are of relatively little importance. The big factors are inhalants and contactants in view of the hypersensitive skin. These can be almost anything that one can think of. Psychological factors become more and more important as the child grows older.

In adulthood, psychological factors are of primary importance and it is often difficult to demonstrate any allergic factors at all.

BASIC ETIOLOGY

All this does not tell us what is really the matter with these people. We know that they inherit something but we do not know what. This is probably in the nature of a biochemical abnormality and Gaddum has suggested that the atopic may really be suffering from an inborn error of metabolism namely a deficiency of the enzyme histaminase. Histaminase which was first discovered by Best has the property of destroying large amounts of histamine and is present in varying concentration in different tissues.

It is known that agents poisoning histaminase sensitize the tissues to the action of histamine (Mongar and Schild). Atopics are hypersensitive to histamine injection, as they develop asthma and hay fever whereas normally there is only flushing of the head and neck (Rose). Evidence of increased release of histamine was shown by Adam who found increased amounts of histamine in atopic urine. Serafini has shown abnormal histamine tolerance curves in a few atopics. All these findings can be explained on the basis of deficient histaminase. The difficulty is that our methods of measuring the in vivo concentration are not

good and results are very variable. The situation somewhat resembles hypersplenism—a beautiful theory but very difficult to prove.

Pathogenesis of Allergy

We have found that there are a great variety of allergic disorders. If we group them according to say their skin test reactions, the results are even more instructive. There are 2 groups.

(*a*) *Early reaction* (5-30 min.)—extrinsic asthma, hay fever, atopic eczema, urticaria.

(*b*) *Delayed reaction* (24-48 hrs.)—allergy of infection, contact dermatitis, drug eruptions, infective or intrinsic asthma.

(*c*) A possible 3rd group are the so-called *"collagen diseases"*. However, in these the evidence for an allergic basis is dangerously thin so that we will not refer to them again.

Within each group there are striking similarities. Between each group there are striking differences.

1. Reactions in both groups are *highly specific* and involve a large number of tissues. In the first these are the skin, bronchi, mucosa of nose and conjunctiva. In the second group with the exception of contact dermatitis, even more tissues are involved, e.g. lungs, kidneys, testes, etc.

2. The results of *skin tests* are quite different. The early reaction occurs in minutes and is a wheal like the triple response. Changes are fleeting and ephemeral and there is never permanent damage. There is no cellular accumulation except for a few eosinophils and the systemic reaction is very acute and disappears rapidly.

In the late reactions there is a latent period of 1-2 days, and wheals do not occur. Changes are more permanent and there is always some evidence of tissue damage. There is a marked cellular accumulation especially of the wandering tissue cells. Systemic reactions are slow in inset, of long duration, and characterized by febrile and general body disturbances.

3. The *characteristic cell* of the early group is the eosinophil. Its functions are quite mysterious. At one time it was believed to release histamine but there is little evidence at present. Perhaps it is merely a scavenger cell attracted by histamine.

The characteristic cell of the delayed group is the lymphocyte or at least the wandering mononuclear. This cell is believed to carry the specific antibody.

4. In the first group the serum contains a substance by virtue of which sensitivity to the specific antigen can be temporarily transferred either locally (as in P-K reaction) or systemically (as in blood transfusion from an asthmatic donor).

In the second group, *passive sensitivity* cannot be transferred by the serum. It can done with mononuclears as has been shown in animals by Chase and in humans by Lawrence. Thus in this group, sensitivity is not dependent upon a serum factor.

5. *Specific histamine antagonists* work well only in the early group and are almost useless in the delayed reactions. The brilliant researches of Sir Thomas Lewis in 1927 showed that the skin responds to injury by the triple response which consists of a red reaction due to dilatation of minute vessels, a wheal due to their increased permeability, and a

flare due to arteriolar dilatation. This is associated with the rapid liberation of histamine or a substance very much like it. The reaction is blocked by the antihistamines which are believed to compete for the histamine receptors on the tissue cells.

However, potassium, adrenaline, and acetylcholine are also substances which can be quickly released by tissue cells and which may contribute to the allergic reaction. Moreover one must be cautious in accepting a histamine basis for any phenomena blocked by the antihistamines for these have other activities which may be involved e.g. atropine like action.

Thus urticaria and hay fever are considered to be due to the release of histamine by the skin and nasal mucosal cells respectively stimulated by an antigen-antibody union; the antihistamines work very well here. There is some doubt as to whether histamine is of any import in asthma as its antagonists do not work well here. However the few cases in which they do work are usually of the extrinsic variety. Perhaps as Sir Henry Dale says, there are 2 kinds of histamine. Extrinsic histamine as in urticaria is released by epithelial cells to act on blood vessels at a distance so that the antihistamines have a chance to compete. Intrinsic histamine as in asthma is released by cell of the shock organ so that the antagonists don't have a chance to interfere.

6. *Cortisone and ACTH* on the other hand seem to have a much greater effect on the delayed reaction than on the early one. It is true that they give excellent results in asthma but it is significant that the best results are in intrinsic or infective asthma. They seem to be of benefit only in the very acute stages of atopic eczema. However the antihistamines are not very effective here either. Atopic eczema is certainly a strange disease. Why do they work? They are certainly not histamine antagonists. They do not prevent the release of histamine for they have no significant effect on the triple response. They do not interfere with the action of histamine for they will not prevent anaphylaxis nor the vasodilatation produced by histamine. Perhaps they prevent the accumulation of wandering cells. Perhaps it is because they decrease capillary permeability. There is some recent work to suggest that the reversal of the tuberculin sensitivity in TB is due to the facilitation of the oxidation of ascorbic acid to dehydroascorbic acid. We really don't know how they affect the allergic reaction.

From all these points, it is evident that there must be quite different fundamental mechanisms at work in the 2 groups. We do not know what these are as yet but the available evidence suggests the following 2 hypotheses.

1. In the early reaction we know that the antibody is outside the cell. Perhaps it becomes adsorbed on the surface of the cell and the contact with the antigen results in the release of histamine or other active substances. Histamine is probably preformed in the cell because the reaction is immediate.

Therefore the early reaction is the result of an antigen-antibody union on the surface of the cell with the resultant release of preformed histamine.

2. In the delayed reaction the antibody is inside the cell. Thus the antigen must penetrate the cell to reach the antibody. Because of the long latent period of 1-2 days, it is probable that the effective substance is not preformed in the

cell but has to be manufactured. The latent period is therefore the sum of the times that it takes the antigen to penetrate the cell membrane, for an enzyme to be released, and for it to complete its work.

Therefore in the delayed reaction, the antigen is phagocytosed by the wandering cells which carry the sensitivity throughout the body. On subsequent contact with the specific antigen, the cells manufacture and release a substance causing vasodilatation and which attracts other wandering cells. These cells appear to be under the control of the endocrine system, especially cortisone and thyroxine.

In conclusion I would like to point out that it is fallacious to consider the allergic reaction as a peculiar manifestation occurring in certain predisposed persons. It can best be understood only as a fundamental mechanism of biologic adaptation.

Acknowledgment

I would like to thank Dr. N. Wrong for his help and encouragement in the preparation of this paper.

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If you wish to fail in the practice of Medicine--Always seek your own interests, make of a high and sacred calling a sordid business, regard your fellow-creatures as so many tools of trade, and if your heart's desire is for riches, they may be yours; but you will have bartered away the birthright of a noble heritage, traduced the physician's well-deserved title of the Friend of Man, and falsified the best traditions of an ancient and honorable Guild.

SIR WILLIAM OSLER

JAUNDICE OF THE NEWBORN—A SUMMARY

MARVIN E. MILLER, 5T5

"Jaundice is, indeed, a mere symptom—and may occur in most diseases of the liver, but it is a symptom so striking, and such an important element in any case in which it may happen, that a separate consideration of it is almost requisite". So commented George Budd in 1846, and to this day the presentation of jaundice constitutes a diagnostic challenge to the physician who must determine the etiology.

Jaundice, or icterus refers to a yellow pigmentation of the skin and mucous membrane which results from an excessive deposition of bilirubin in the epidermal germinating layer. Because heredity and environment can themselves influence skin colour—much embarrassment (especially to the budding diagnostician) can be avoided if the sclera are examined, for it is here that yellow pigmentation almost certainly is indicative of jaundice.

The Blood Picture:

Normal serum contains from 0.2–1.0 mg. bilirubin per 100 cc. This results from physiological breakdown of red blood cells. However, in cases where there is (1) an excessive breakdown of R.B.C. or (2) a barrier to the flow of bilirubin in bile into the duodenum—there results a hyperbilirubinemia which ultimately causes staining of tissues.

Mode of Production and Classification:

Bilirubin is the chief pigment contained in bile. It is formed as a breakdown product of hemoglobin by the reticulo-endothelial cells of the body and chiefly of the bone marrow. The liver can be thought of as a central receiving and relay depot in which the portal and hepatic blood is relieved of its products. The product we are interested in—bilirubin—then passes through the liver cells, becomes integrated in bile and is then "shipped" via intrahepatic bile canaliculi, larger hepatic ducts and finally the common hepatic duct to the gall bladder through the cystic duct.

Considering the liver as a focal point of entry and distribution, it can be seen that jaundice could be produced as a result of prehepatic, intrahepatic or posthepatic pathology with regard toladening the blood excessively with bilirubin. Or as Boyd puts it very simply—"in jaundice the essential pathology may lie *before, in,* or *after* the liver cell." Using this principle as a basis of differential diagnosis there have been a number of equally good classifications of jaundice elucidated. One of the most recent is that already given which has been advanced by Ducci. He lists the 3 types of jaundice as

(1) Prehepatic—which includes the various types of hemolytic and constitutional hepatic dysfunction.

(2) Intrahepatic — which includes hepato-cellular and hepatocanalicular forms.

(3) Posthepatic—which includes the benign and malignant varieties of obstructive jaundice.

It has been suggested by Rich, that in the case of hemolytic jaundice, the mani-

festations occur not simply due to an excessive breakdown of Hb., but is associated usually with some form of hepatic insufficiency. In other conditions of obstructive and septicemic jaundice—the liver cell damage component is also in evidence.

The Van den Bergh Reaction and its Significance:

This is a laboratory test used to indicate the nature of bilirubin in blood serum. It makes use of 2 reagents made up in solution which are then mixed and to 1cc. is added 1cc. of blood serum. Whether or not a reddish violet reaction occurs promptly or requires the addition of alcohol to bring it about will depend upon what has happened to the bilirubin in its formation. The two reactions are called (a) direct and (b) indirect. The former exhibits 3 types of reactions—(1) immediate (2) delayed (3) biphasic but all appear without the addition of alcohol. It has been suggested that the serum bilirubin of both intrahepatic and posthepatic jaundice gives a direct reaction because the bilirubin has passed through the liver cells. In the liver cell, some substance (possibly bile salts) reacts with bilirubin to break down a bilirubin $\begin{matrix}\text{-protein?}\\ \text{-lipoid?}\end{matrix}\Big\}$ linkage and thus permits the pigment to appear in serum in the free state which allows it to react directly with the diazo reagent of the test. The bilirubin of prehepatic jaundice has not been so disrupted from its complex and alcohol is required to bring about the reaction, and is thus an indirect reaction.

Another view is that bilirubin of the direct reaction is converted in the liver cell to an alkali salt which is soluble in water, whereas that of the indirect reaction remains an acid pigment which is insoluble in water but is soluble in alcohol. Be that as it may, the fact still remains that the test is usually indicative of whether or not the liver cell has been involved in bilirubin transfer, and thus is helpful in a differential diagnosis.

With this cursory glance at the subject of jaundice as a whole, we can now look at some conditions both physiological and pathological that manifest themselves as congenital icterus.

(1) Physiologic Jaundice:

PRE-HEPATIC

$$\text{Hb Breakdown} \longrightarrow \begin{matrix}\text{Bilirubin}\\ \text{Excretion}\end{matrix}\Big\{\begin{matrix}\text{Liver}\\ \text{Kidney}\end{matrix}$$

A normal occurring jaundice results following an excessive prenatal erythrocyte formation. There follows in the 1st few days post partum (1–6) the manifestation of jaundice due to excessive blood bilirubin. This is hemolytic in formation and occurs because the increased R.B.C. level is not now required by the independently respiring infant. A balance is set up between the breakdown of R.B.C. to form bilirubin and its excretion by the liver and kidney.

It has been shown that the cord blood bilirubin content is higher than that of material blood and the peak of bilirubin reached after birth is related to the bilirubin content of cord blood. Usually the intensity of jaundice is correlated directly with the time that the condition is present. With premature birth it is found that the infants exhibit jaundice more often and that it is of increased severity over that of full term babies. With this type of jaundice, physical findings, other than that of yellow pigmentation, are not pre-eminent.

(2) Erythroblastosis Foetalis:

ETIOLOGY

It is now well established that isoimmunization of maternal blood by one of 2 factors causes the formation of antibodies which traverse the placenta and cause an antigen—antibody reaction to occur in fetal R.B.C. which leads to a pathological hemolysis of the cells. Isoimmunization is the reaction of antibody formation to the presence of antigen found in some members of the same species which by some route enters the circulation of the recipient blood. Rh incompatibility is the factor involved in over 90% of cases. Rh —ve women with an Rh +ve fetus (husband is Rh +ve) may develop antibodies to the Rh antigen. The antibodies combine with fetal Rh +ve R.B.C. to precipitate the hemolytic reaction. Also women who have been previously transfused with Rh +ve blood will possess antibodies to this factor and these in turn can bring about a similar hemolytic breakdown of cells. The remaining cases are accounted for by other constellations of blood group incompatibility. The Rh factor in relation to antibody formation is a subject in itself and cannot be dealt with here. However the icteric condition that results, shows severe manifestations which can be briefly elucidated. Because of severe uncontrolled hemolysis there is little or no balance between breakdown and excretion. Thus:

PRE-HEPATIC

Hb Breakdown → Gross Accumulation of Bilirubin

PATHOLOGY:

(1) Widespread hemopoiesis of great degree in bone marrow, spleen and liver.
(2) A blood picture resembling severe macrocytic anemia, low red count, nucleated erythrocytes, platelets markedly decreased, R.B.C.-macrocytic, Hb may be high.
(3) Hepatomegaly and splenomegaly.
(4) Petechiae of serous and mucous surfaces and massive pulmonary hemorrhages (sometimes is the immediate cause of death).
(5) Kernikterus—pigmentation of basal ganglion.
(6) Placenta—edematous and showing erythropoietic activity.

The intensity of jaundice may not exceed physiological proportions but often it is of severe intensity—the skin showing a deep orange colour which may later change to a greenish hue. There is usually severe edema and anemia. Other symptoms and signs include listlessness, a feeble cry, cyanosis and respiratory distress, petechiae and ecchymoses.

PROGNOSIS:

Death may occur within the first day of life. In other cases the jaundice subsides gradually and most children recover completely. There may be remnants of the disease in the form of mental retardation, spastic paralysis and choreoathetotic movements.

TREATMENT AND MANAGEMENT:

Replacement of lost erythrocytes is the best treatment but its instigation should be based on the degree and progress of the anemia. Naturally, replacement therapy makes use of Rh —ve blood only, since it is the Rh +ve cells that are being destroyed in the hemolytic process. Oxygen administration is made use of in cyanotic cases, and Vitamin K intravenously administered is indicated in cases where the prothrombin time is prolonged. Up until the 7th month of

intrauterine life, antibody absorption by fetal cells is negligible. Therefore in cases suspected of resulting in a possible erythroblastotic infant by the use of parental blood tests, premature delivery may be undertaken. This, however, tends to precipitate further perils as for any premature child and so should be carefully contemplated.

The subject of erythroblastosis leaves room for wide speculation when it comes down to predicting the condition of a child born of Rh —ve mothers and Rh +ve fathers. In general the incidence of the condition is comparatively low for statistics show that parents with the above blood picture comprise 10% of the married population. The first born is rarely afflicted. But in families where there is a tendency for the disease to occur more frequently it also occurs with increasing severity in the subsequent children.

(3) Congenital Atresia of the Bile Ducts:

INTRA- AND POST-HEPATIC

Obstruction Bile Flow	→	Circulation Hyper Bilirubinemia

This rare condition occurs when for some reason there is a failure of intrahepatic and possibly extrahepatic bile ducts to canalize. It manifests itself as an intense jaundice becoming noticeable in the 2nd or 3rd week of life and subsequently fluctuating in intensity. The colour is yellowish at first but later takes on a greenish hue which never quite disappears. The stools are acholic or light in colour, the liver is enlarged and firm and there is usually splenomegaly. The condition of the child is good for several months of life, but as is true of obstructive jaundice in general, the itching may be intense. Occasionally xanthomatous lesions containing cholesterol develop in the skin due to the high serum cholesterol content. The prothrombin time is greatly prolonged and the urine is highly coloured while the stools are acholic or pale.

Jaundice with obstruction of biliary passages may result as a late complication of erythroblastosis. Its manifestations are essentially the same as congenital atresia. For both conditions surgical intervention is required. Secondary measures include parenteral administration of Vitamin K and general supportive measures.

(4) Septicemia:

PRE-HEPATIC AND HEPATIC

Hemolysis	→	Hyperbilirubinemia
Functional Hepatic Immaturity	→	

This condition does not occur very frequently. When it does, the causative organisms have been shown most frequently to be Staphylococcus and B. Coli. The pigmentation occurs usually 3 days postpartum and may increase uninterruptedly. This type of icterus in the newborn appears to be related to the functional immaturity of the liver rather than any extensive hemolysis. The results of infection include cutaneous, umbilical and hematogenous infection. Occasionally milk borne or respiratory infections are the etiological pathways. In this condition, the symptoms include jaundice—along with pyrexia, cyanosis, toxicity, and vague irritability. Bacteriological procedures reveal positive blood cultures.

Two other septicemic conditions associated with jaundice have been reported recently having only occasional frequency. They are:

(1) *Buhl's Disease* — an intrauterine bacterial infection which exhibits cyanosis, hemorrhagic tendency, jaundice and evidence of intravascular hemolysis along with fatty degeneration of all organs.
(2) *Winckel's Disease*—a postuterine infection characterized by hemolytic jaundice and methemoglobinemia.

We have seen that jaundice in the newborn is manifested as in the adult because of pathology "before, in, or after the liver." It may be mentioned that congenital syphilis simulates any phase of Erythroblastosis but can be differentiated on the basis of history, syphilitic signs, blood tests and X-ray of long bones.

In summary—we can consider the following table.

Acknowledgement

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Disease	Degree of Jaundice	Blood Picture	Hemopoietic Organs	Lab Investigation	Essential Pathology
Physiologic Jaundice	(1) Variable but usually not severe. (2) Disappears in 2 or 3 weeks.	Unaltered	Normal	*Van den Bergh* (1) Indirect (2) Urine and stools normal	
Erythroblastosis Fetalis	(1) Early appearance (2) Can be very intense	(1) Macrocytic anaemia (2) Rh incompatibility —agglutinating or blocking antibodies	Hepato- and Splenomegaly	(1) V. den Bergh —indirect at first —direct later (2) Urine and stools are strongly coloured	Prehepatic
Congenital Atresia and Mechanical Obstruction	(1) Onset is late (2) Intense	Unaltered	Hepatomegaly Splenomegaly (occasionally)	(1) V. den Bergh is direct (2) Stools are acholic (3) Prolonged prothrombin time	Intra- and Post-hepatic
Septicemia	(1) Onset 3rd day post partum (2) Continues if unchecked	—Leucocytosis —"toxicity"	Unaltered	(1) V. den Bergh—indirect (2) +ve blood culture	Prehepatic & Hepatic

A REPORT ON SEVEN CASES OF DIPHTHERIA

A. STANLEY, M.D.*

Preliminary Discussion

This is a report of seven cases of diphtheria to remind the reader of the existence of the disease, its seriousness, and its variability. I say to remind the reader because to many younger physicians, this is an uncommon disease.

This report is written because in six undergraduate years, I did not see a single case of diphtheria. Prior to the cases below, the only case I had seen was in my first interne year. At that time a child came into the Emergency Room with severe tracheitis and indrawing, and in spite of all treatment died two hours later. At autopsy, the diagnosis of diphtherial laryngitis was made. This case broke the Health Department's perfect record for two and a half years in a city of one million people.

Diphtheria, is by definition, an acute infection and contagious disease, caused by a gram positive rod, the corynebacterium diphtheriae, (Klebs-Loeffler bacillus), (bacillus diphtheriae), characterized by toxemia and a fibrinous membrane on the mucous membrane of the respiratory tract.

Contact may be direct or indirect, mainly the former, as respiratory droplets. The incidence is from one to ten years, the maximum being two to five. The incubation period is one to seven days. The mortality rate is five per cent or lower for naso-pharyngeal types but is considered to be approximately fifteen per cent in laryngeal cases. With the advent of the present antibiotics, it is believed that the mortality rate is slightly less than these figures quoted in 1946.

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Case Reports:

CASE NO. 1: M.G.R., female child, 13 months, admitted 10/24/52.

Chief complaint: Difficulty breathing.

History of present illness: The patient had a one month history of intermittent nasal discharge and malaise. Two days prior to admission, the patient had a running nose with scabs both in the nose and on the upper lip resembling herpes-simplex. This was associated with an increased respiratory stridor and shortness of breath. The patient had an elevated temperature of 103 but no history of pain, cough, sputum, or hemoptysis. No history of congenital heart disease, palpitation, tachycardia, swelling of the ankles, or cyanosis. No previous history of rhinitis, hayfever, or other allergic nasal conditions.

Family history: The family history revealed that one cousin had a history of diphtheria three weeks previously. This cousin was apparently treated in another hospital and nothing was known about the patient or his progress. No other significant family history was obtained.

Past history: The past history revealed that the patient had been in good health all of her life, until the onset of the present illness.

Functional inquiry: There was no significant history on functional inquiry

beyond the symptoms described in the history of present illness with one exception. There was, on the back of the right leg, one inch above the knee crease, an area about two inches in diameter resembling an apple-jelly, colored pink, which was considered to be an area of cellulitis. This had been present for approximately one week, otherwise, the extremities were negative.

Physical examination: The patient was a 13 month old white female child, irritable with notable scabs on the upper lip and in the nostrils.

Examination of the skin was negative except for an area of cellulitis two inches in diameter above the right skin crease posteriorly of the right knee.

The head and scalp were normal. The eyes were moist and hazy and reacted to light and accommodation. The ears were clear; there was no evidence of otitis media or external infection; hearing was good. The nose was injected and the scabs mentioned previously were noted. These were both on the upper lip and in the nose and resembled herpes simplex. Examination of the mouth, both fossae, tonsillar beds and pharyngeal wall, revealed these covered with a grayish exudate. Several white plaques, oval in shape, approximately 1 cm. times ½ cm. were seen in the fossae and pharyngeal wall. The remainder of the pharynx and fossae were injected. No other abnormalities were noted.

The neck was normal; no glands were enlarged. There was no stiffness, redness, swelling, torticollis, or venous enlargement.

The thoracic wall was normal. The lungs were normal to percussion, auscultation, and external examination with the exception of tubular breathing, and a few occasional rhonchi present bilaterally. The heart and vascular system, including the blood pressure, were normal. No abnormalities were found on examination of the abdomen and genito-urinary tract. The anus and rectum were normal. The glandular system throughout the whole body, was normal and was not enlarged. The bones, joints and muscular system and nervous system showed no abnormalities.

The diagnosis on admission was nasopharyngeal and laryngeal diphtheria.

Laboratory work: A smear and culture for diphtheria was made immediately on admission. The smear was believed to be negative for diphtheria. The urine was essentially negative. The hemoglobin was 11 gms., 3,800,000 RBC, and 22,600 WBC. There was a slight increase in the neutrophiles but otherwise the differential was normal. Twenty-four hours later, the culture was reported positive for diphtheria.

Course and treatment: The patient was given 20,000 units of diphtheria antitoxin on admission intramuscularly because of her clinical appearance, and in spite of a negative report on the appearance of the smear for diphtheria. A similar dose of antitoxin was repeated four hours later. On admission the child was also given 100,000 units of crystalline penicillin and 300,000 units of Duracillin. The Duracillin was ordered b.i.d. Over the next 12 hours, the shortness of breath and respiratory stridor increased, with slight indrawing noted at this time. An ENT consultation was ordered and a tracheotomy set was put by the bedside. Oxygen and croup tent were started immediately. On the following day, the culture was reported as posi-

tive for diphtheria. The patient's temperature was 103 on admission, fell to 99 by 12 p.m., ten hours after admission. Two hours later it had risen to 101. The temperature ranged between 101 and 102 on the second day of admission. Because the child's condition had not improved in 48 hours, the Duracillin was discontinued and the child was put on crystalline penicillin 100,000 units every four hours. An additional 20,000 units of diphtheria antitoxin were given intramuscularly at this time. Over the next 24 hours the temperature fell and remained between 99 and 100. These were rectal temperatures. The fourth day following her admission, the temperature ran at 99 rectally, which was considered normal. The temperature remained at this level during the remainder of her hospital stay.

The patient improved clinically, on the fourth day of hospital admission. The breathing became less difficult, shortness of breath decreased, and the patient gradually improved. The last six days of hospital admission, the patient looked well. Five days prior to the discharge of the patient, the antibiotics were discontinued. Two days following the discontinuation of antibiotics, throat swabs were taken twenty-four hours apart. Both of this were reported as negative for diphtheria. The child was kept in the hospital for three days following the negative report and then was discharged home to bed, under the care of the family doctor.

While in the hospital the skin lesion cleared on the third day. The question as to whether this was a staphylococcus infection or an associated diphtheria skin lesion was unanswered. The patient was discharged on 11/7/52. The child's progress three weeks after discharge, was reported as "good".

CASE NO. 2: W. D. R., age 6, white child.

The patient was admitted on 10/25/52, discharged 10/30/52 to his home. The second patient was the brother of the first patient, and was picked up by routine investigation in the home following the admission of the first child.

Chief complaint: Fever of 101 degrees. *History of present illness*: The child had been in good health until the evening prior to admission, when his mother had noticed that he had a mild temperature. He had been playing and in no way felt ill.

Family history: This patient had a sister age thirteen months with diphtheria, and a cousin previously reported with diphtheria.

Past history: The patient had been in excellent health. The mother states that she had him routinely immunized three years previously. The Public Health Department, however, have not verified this statement.

History of present illness: The patient had no history of sore throat, sore ears, difficulty in breathing, pain, cough, sputum, or hemoptysis.

Functional inquiry was entirely negative.

Physical examination: A well nourished, well developed, white, male boy, apparently not acutely ill or in any distress. The skin was flushed, warm and dry. No abnormalities of the head were noted. The eyes reacted to light and accommodation and had a full range of movement. Examination of the ears was negative. There was a moderate congestion of the nose, otherwise, the examination was negative. The throat and tonsils were generally inflamed and slightly swollen. The tonsils were (three plus) enlarged

with white plaques but no membrane. A single, non-tender, lymph gland without swelling or redness, was present below the right mandible. Otherwise, the examination of the head and neck was normal. The examination of the thorax, lungs, and the heart, revealed no abnormality. The abdomen and G. U. system were normal. The examination of the anus and rectum was deferred. The glandular system was normal except for the one gland, described as above, in the neck. The bones, joints, and muscular system were normal. The nervous system showed no abnormality.

The admitting diagnosis was an acute pharyngeal-tonsillar diphtheria.

Laboratory work: The smear was suggestive of diphtheria and this was confirmed twenty-four hours later by culture. The urine was essentially negative. The hemoglobin was 71.4%, 3,880,000 RBC, and 9,400 WBC. The differential was normal.

Treatment: Forty thousand units of diphtheria antitoxin were ordered intramuscularly over four hours. However, the cutaneous test dose, gave a red reaction in twenty minutes, and the order for diphtheria antitoxin as above, was cancelled. Twenty thousand units of diphtheria antitoxin were given intramuscularly, one tenth of a cc., every two hours. In addition, the child received duracillin, 300,000 units intramuscularly stat, and b.i.d.

Course: The child's temperature was 101 on admission and it fell rapidly to normal in 36 hours. The temperature remained this way for the remainder of the hospital admission. Clinically the child looked well. Because of economic conditions, the child was discharged home under the supervision of the Public Health Department on 10/30/52.

* * *

CASE NO. 3: E. J. I., Age 3, white child, admitted 10/25/52, discharged 11/5/52.

Chief complaint: Slight cold with sore throat.

History of present illness: This child came from the same geographic locality as the previous two children with diphtheria. The child was brought to the Emergency Room by the parents mainly because of this reason. The child had a running nose and sore throat but no history of earache, otitis media, difficulty breathing, pain, cough, sputum, or hemoptysis. There were no cardiac or G. I. complaints. The child felt well except for the cold and the remainder of the functional inquiry was entirely negative.

Family history was non-contributory.

Past history: The child had always been in good health.

Physical examination: A well nourished, well developed, white female child, with no rashes or evidence of abnormality of the skin. The head and scalp were normal. The eyes reacted to light and accommodation with a full range of movements and no evidence of infection. On the examination of the throat, there was a small white plaque, one cm. times ½ cm., on the right tonsil suggestive of diphtheria. The pharyngeal wall was slightly injected as were the fossae. The naso-mucosa was slightly injected, and a serous discharge was noted. There was no pain, tenderness, swelling, redness, difficulty moving the neck, masses or glands palpable. The thorax was normal in contour and the lungs and heart

showed no abnormality. The abdomen was soft, non-tender, non-rigid, without masses. There were no herniae. The G.U. system was normal. The rectal examination was negative. The glandular system was normal throughout. The bones, joints, and muscular system, showed no abnormalities and the nervous system was normal. The child's temperature was 100 on admission.

The admitting diagnosis was tonsillar diphtheria.

Laboratory work: The urine was essentially negative. The hemoglobin was 74.1%, 3,900,000 RBC, and 8,000 WBC. The differential was normal.

Clinical course and treatment: The child was given diphtheria antitoxin 20,000 units intramuscularly on admission. This was repeated in four hours. Duracillin 300,000 units was given daily. The child had continued to look well. The antibiotics were discontinued on the 11/1/52. A throat culture was taken three days later and repeated in twenty-four hours. These were negative. The child was discharged home on 11/5/52 as recovered.

* * *

CASE NO. 4: L. M. K., 5 year old, white girl.

The patient was admitted in the Emergency Room on 11/7/52, took two breaths, and died before medical help could be obtained.

History of present illness: This five year old, white female child, was well until twenty-four hours prior to admission. At this time, she had a cold and a sore throat. She was kept at home until one half hour prior to admission, when she began to choke. The mother tried to remove the phlegm from the child's throat with her finger, but was bitten, so brought the child to the Emergency Room, where she died before help could be rendered.

Physical examination: On examination, a lifeless white female child was seen; no gross abnormalities were found. On examination of the throat, a brown liquid fluid was seen, resembling regurgitated stomach contents. Cultures were taken from this fluid and the diagnosis of diphtheria was made.

A consent for autopsy was not given and it was felt that the diagnosis of laryngeal diphtheria, with strangulation was sufficient to account for the child's death.

* * *

CASE NO. 5: Baby E. B., 2 year old colored male child.

Chief complaint: Shortness of breath.

History of present illness was inadequate. The mother left before a history could be obtained, and she was not seen until the child's discharge, and then unfortunately not by a doctor. However, it was known that the child had been ill at least twenty-four hours, and had been treated twenty-four hours previously with penicillin, and 10,000 units of diphtheria antitoxin. The child had been seen again twelve hours later and 10,000 units of antitoxin and another dose of penicillin had been administered. The patient had not improved and was admitted to the hospital. No family or past history was obtainable. On admission the child had a temperature of 102.

Physical examination: A well nourished, well developed, colored male child, hydrated but with severe respiratory distress

was seen. The examination of the skin was normal. The head contour was normal. There was a moderate infection of the scalp, of fungus origin. The eyes reacted to light and accommodation. There was a full range of movements and no evidence of infection. The nose and ears appeared normal. However, the throat was full of thick tenacious mucous which was difficult to remove. It was impossible to visualize the land marks of the throat. Swabs were taken. Examination of the neck revealed a bilateral adenitis without tenderness or redness. No pain or swelling with the exception of the adenitis was noted. The thoracic cage was normal. Examination of the lungs revealed tubular breath sounds bilaterally with associated rhonchi. No rales were noted. No dullness was noted on percussion at this time, but two hours later, dullness of the right lower lobe was noticed. Fremitus was increased on the right side. The heart rhythm and the rate were regular and no adventitious sounds were heard. The blood pressure was normal. The abdomen was soft, non-tender, non-rigid, without any masses or herniae. The G. U. tract and rectum were normal. The glandular system was normal except for the bilateral cervical adenitis. The bones, joints, muscular system, and the nervous system were negative on examination. The diagnosis of acute laryngeal tracheitis was made on admission and two hours later, the diagnosis of right lobar pneumonia was made. Twenty-four hours later, the diagnosis of acute diphtheria laryngeal tracheitis was made with pneumonia.

Laboratory work: On admission the urine was grossly normal. The microscopic examination was normal. The hemoglobin was 64.9%, 3,340,000 RBC, and WBC of 25,400 with a normal differential count. Cultures for diphtheria were positive in twenty-four hours.

Treatment: The decision to treat the child on terramycin was made with the view of observing the effect of this drug on the condition. Unfortunately a mistake was made, and penicillin was given also. On admission the child was given a elixir terramycin, dms. 1, stat, dms. ½, every six hours, 100,000 units of crystalline penicillin stat and 300,000 units of duracillin administered daily. Intravenous fluids were given and the temperature fell rapidly from 102 to 100 in twenty-four hours. The temperature remained approximately at this level for the next three days. Twenty-four hours after admission, the culture showed a positive test for diphtheria, so diphtheria antitoxin, 20,000 units intramuscularly, was given and repeated in four hours. The chest X-ray revealed extensive lobar pneumonia on the right side.

Course: Four hours after admission, the throat was eventually cleared of mucous, both tonsils, fossae, and pharynx, were seen to be congested, swollen, and red. Twenty-four hours after admission, re-examination, revealed two white plaques, one half by one half cm. on each tonsil. The examination of the chest was the same as the night before except the pneumonia was now of typical lobar-distribution. The oxygen and croup tent started on admission, were discontinued on the third day after admission. Five days after admission, penicillin was discontinued, and three days later, the terramycin was discontinued. Clinically the patient improved after the first forty-eight hours. The temperature, which on admission, was 102, fell to 100 in the first twenty-four hours and remained at this level for the first six days. On the seventh day, the temperature fell to 99.6 rectally and

remained at this level for the remainder of the hospital stay. After the seventh day, the chest cleared almost completely, with occasional rales and rhonchi heard until the fifteenth day of hospital admission. An X-ray at this time, revealed improvement in the chest but that evidence of pneumonia still existed. Cultures taken two days after discontinuation of the antibiotics, were negative for B-diphtheria. They were repeated twenty-four hours later, and also were reported as negative. An EKG taken at this time, was reported as normal. Clinically, the child had looked well for ten days. However, because of the occasional rales in the chest, the X-ray appearance of the chest, and a slightly elevated sedimentation rate, the child was investigated for tuberculosis. This investigation was negative and the child was discharged on 12/3/52, completely recovered.

* * *

CASE NO. 6: M. E. B. An eight year old, colored female, child.

Chief complaint: Shortness of breath. Like the previous case, because of incompetency of the nursing staff, the mother left before a history was obtained by the doctor. No history was obtainable in this case and the mother could not be reached by phone. No family history or past history was obtainable in spite of the child's age.

Physical examination: An acutely, ill, colored, female child, was seen with marked shortness of breath. There was a rash over the lower abdomen and extremities, resembling multiple mosquito bites. Otherwise, the skin showed no abnormalities. The head was normal in contour. The eyes were clear, reacted to light and accommodation, and had a full range of movement. There was a clear nasal discharge with injection of the mucosa but no bleeding or other abnormalities of the nose. The tonsils and pharynx were congested and there was a white membrane over the left tonsil. There was a moderate amount of white mucous in the throat and no other abnormalities were noted. The examination of the ears was negative. No glands were palpable in the neck but there was thickness of the neck which was considered due to edema. There was no pain, tender, redness, or rigidity, etc. The thorax was normal; the lungs were clear to auscultation and percussion. The heart rate was regular but the rate was rapid (96). There were no adventitious sounds heard. The abdomen was soft, non-tender, non-rigid without masses, the liver was just palpable but not beyond normal limits. There were no herniae present and the examination of the anus and rectum was deferred. There were no complaints of the genital urinary system and it was felt that the glandular system was normal. Examination of the bones and joints, muscular system, and nervous system, revealed no abnormalities. The admitting diagnosis was pharyngeal and tonsillar diphtheria.

Laboratory work: The urine was essentially negative except for an increase in protein and a white blood count of 22 cells. The hemoglobin was 12.5 gms., RBC 4,200,000, WBC 22,600, with a normal differential. Throat cultures on admission and two days later, were positive for staphylococcus aureus but were negative for B-diphtheriae. They were sent to the State Health Department as a check and were later reported as positive for diphtheria.

Treatment: Because of the clinical appearance of the child, 20,000 units of diphtheria antitoxin were given intramuscularly, stat, and this was repeated in four hours. An attempt was made to

run a series on terramycin, so terramycin, elixir, dms. 1, was given stat and was repeated in six hours and then ½ dm. was given every six hours.

Course: The child's temperature, which was 103 on admission, dropped to 99 in thirty-six hours and ran between 99 and 100 for the next forty-eight hours. Following this the temperature remained at 99 rectally. The child appeared to improve after the first twenty-four hours, but did not look clinically well until the fourth day after admission.

Comment: The swabs for culture, in this child, were not taken as carefully from the edge of the membrane as had been done in the previous five cases. Clinically, this appeared to be another case of diphtheria, much more typical than the fifth case. However, this was never proven.

* * *

CASE NO. 7: V. B., two year old, male, colored child.

Chief complaint: Difficulty in breathing.

History of present illness: History of a severe cold, for five days. Twelve hours before admission, the patient was taken to a doctor, who gave him two "shots" of unknown origin, and sent a swab to the laboratory in the hospital. The diagnosis of diphtheria was made by the laboratory. The patient was admitted to the Emergency Room with marked dyspnea, wheezing, and a whitish membrane forming on the tonsils.

Family history: Non-contributory.

Past history: The child had been in good health except for measles.

Functional inquiry was negative except for the history of present illness.

Physical examination: A two year old child, having difficulty in breathing, wheezing, with a temperature of 104 was admitted. There were no abnormalities of the skin, and the head contour was normal. The eyes reacted to light and accommodation and had a full range of movement. There was no injection. The nose was injected but otherwise was normal. The ears were normal. The pharynx was injected. The tonsils had a whitish membrane bilaterally. There was a mild adenitis, bilaterally, otherwise the neck showed no abnormalities. The chest was clear except for some tubular breathing. The heart was regular, the rhythm was unaltered, and the heart rate was rapid, (94). No adventitious sounds were heard; the blood pressure was normal. The abdomen showed no abnormalities nor did the G. U. tract or extremities. The neurological was normal. The bones, joints, and muscular system showed no abnormalities. The admission diagnosis of diphtheria was made.

Laboratory findings: The hemoglobin was 80%, RBC 3,900,000, WBC 10,000 with a normal differential. Cultures were positive for B-diphtheria. The cultures taken ten days later, twenty-four hours apart, were negative for B-diphtheria.

Treatment: The child was given 20,000 of diphtheria antitoxin intramuscularly stat, 100,000 units of crystalline penicillin were given immediately and then 50,000 units were given every four hours. The patient was placed in an oxygen tent. Four hours later, the antitoxin was repeated. Eight hours later the antitoxin was repeated and the crystalline penicillin was increased to 100,000 units every four hours.

Course: The temperature dropped from 104 on admission to 101 and ranged between 100 and 101 on the second day of admission. On the fourth day it fell

to 99 rectally and stayed at this level throughout the remainder of the hospital course. The child remained in oxygen for three days but improved sufficiently at this time that it was felt safe to discontinue this form of treatment. The membranes sloughed typically and after the fifth day, the child looked well.

Discussion:

Follow-up in the community: Seven cases of diphtheria have been reported briefly. The first three came from a dairy farm. The examination at the farm, revealed two other cases, which were treated at home. All seventy people on the farm were given antitoxin or toxoid as the case indicated. It was felt, at that time, that the disease was wiped out in this area. No evidence could be found to incriminate the milk or water. The transmission was believed to be due to a carrier.

The fourth patient, who died, was in a town, twenty miles away. No connection could be found between the two outbreaks. Examination in this latter community, revealed that this child's brother had diphtheria. He was treated at home and was given penicillin and diphtheria antitoxin on the first day after diagnosis. The second day, when the doctor visited the family, he had found that they had left to bury the fourth patient in West Virginia and a warrant was sent out for their arrest. They were not found until one week later, when they returned to Virginia. Swabs taken at this time were negative for diphtheria, but the boy was treated with penicillin and antitoxin as a prophylactic measure. The last three cases on discussion, came from an area of a five mile radius in a city of 20,000. The brother of one of these was found to have diphtheria and he was treated successfully at home.

Manifestations of diphtheria in these cases: The faucial manifestations of diphtheria were present in all cases. The onset in all but two cases, was insidious with slight soreness of the throat, malaise and low grade fever. In two of the cases, the pulse rate was increased and in the others, it was normal.

In three of the cases, the diphtheritic membrane was typical but in the others it was atypical and resembled the white plaques seen in monilia. No attempt was made to remove the membrane. However, when swabs were taken, in three of the cases, bleeding occurred. Separation of the membrane, in most of the cases occurred typically, during the course of the disease.

In the first case, the patient was felt to have nasal diphtheria, one other manifestation of the disease. In two other cases there was a marked nasal discharge, cause unknown. In one of these cases, there was marked edema and swelling in the anterior and lateral parts of the neck. However, no lymph glands were felt through this swelling.

If the sixth case can be considered that of diphtheria, five of the cases had laryngeal involvement. All of these had some degree of hoarseness and two of these had mild indrawing which disappeared within eight hours of treatment.

No lesions of the skin were noted unless the lesions of the first case were that of diphtheria. No evidence of cardiovascular diphtheria was noted. In most of the cases, an EKG was taken and these were found to be negative. Unfortunately, this was not done routinely. We regret that an autopsy was not done on the case that died, as the extent of the diphtheria in this case will never be determined. There was no evidence of peripheral neuritis in any of the cases.

The so-called, mousy odor, as is suppose to be characteristic of diphtheria, was never noticed. The differential diagnosis of croup was held in the fifth case; this proved to be diphtheria.

In the sixth case, the diagnosis of diphtheria was made but never proven* and it was quite probable that this was a staphylococcal laryngotracheal-bronchitis. We do not feel that one can differentiate between the diphtheritic and other forms of tracheitis.

Treatment: Most of the patients were treated with diphtheria antitoxin and penicillin. One case was treated on terramycin but unfortunately got penicillin as well. This child's course ran much the same as those on penicillin alone. One child was treated on terramycin alone. The course in this particular case also followed the pattern of the others. However, this was the case in which diphtheria was never proven.* No reaction was noted with the antitoxin, and the one child who showed sensitivity, was given small doses of antitoxin without any apparent harmful effects.

In the two cases of indrawing, tracheotomy sets were placed at the bed side and because of the rapid improvement, they were not needed.

All cases were treated by isolation technique. The patients were given a fluid diet during the serious, acute portion of the illness, gradually increasing to a normal diet, as the child improved clinically.

Because we have not run a series on terramycin or other drugs, we concluded that penicillin is still the drug of choice. We see no reason for using it alone and feel that the antitoxin is definitely of benefit.

*Since writing, this case was proven.

SUMMARY:

This is a report on seven cases of diphtheria to remind the reader that this is a serious disease often fatal, and may be easily preventable by immunization.

Its seriousness is revealed by the death of a five year old girl. The rapidity of this child's death, with only a twenty-four hour history, compared to the two children with proven diphtheria, but without symptoms beyond a mild fever, (temperature of 100) shows the variability of the disease. The fifth child with the thick mucous in his throat, diagnosed on admission as acute pharyngeal-tracheitis, possibly staphylococcal in origin which proved to be diphtheria, shows the confusing clinical picture. Numerous patients with this picture but without tracheitis, are treated in the home by general practitioners with antibiotics and the patients promptly recover in twenty-four to forty-eight hours.

In the seven cases reported here, five had tracheal involvement and of these, one died, which is a mortality rate of 20%. Two others had faucial diphtheria, and ran a mild course. Of the four cases mentioned who were treated at home, they were all faucial and all ran a mild course. The mortality rate in these cases was zero.

Penicillin is still the drug of choice and treatment with diphtheria antitoxin is recommended.

I feel, in conclusion that this is an extremely lethal disease, that immunization is of extreme importance, that active immunization should be compulsory, and I hope that these seven cases may be a spur reminding physicians of the seriousness of diphtheria and of the necessity of immunization.

RECENT ACCESSIONS TO THE MEDICAL READING ROOM

February 1953

Antiobiotics; a survey . . . by H. W. Florey and others. v. 1–2, 1949.
Beckman, H.: Pharmacology in clinical practice. 1952.
Bell, E. T.: Textbook and pathology. 7th ed. 1952.
Black, D. A. K.: Sodium metabolism in health and disease. 1952.
Cullen, S. C.: Anesthesia in general practice. 1951.
Davson, H.: The permeability of natural membranes. 2nd ed. 1952.
Davson, H.: A textbook of general physiology. 1951.
Dubos, R. J.: Bacterial and mycotic infections of man. 2nd ed. 1951.
Maxwell, J.: Introduction to diseases of the chest. 3rd ed. 1948.
Gibbs, F. A.: Atlas of electroencephalography. 2nd ed., vol. 2, 1952.
May, R.: The work and training of the psychological therapist. 1950.
Mazer, C.: Diagnosis and treatment of menstrual disorders and sterility. 3rd ed. rev. 1951.
Medical Research Council: The Rh blood groups and their clinical effects.
Moore, F. D.: The metabolic response to surgery. 1952.
Rivers, T. M.: Viral and rickettsial infections of man. 2nd ed. 1952.
Strecker, E. A.: Fundamentals of psychiatry. 5th ed. 1952.
Strecker, E. A.: Practical clinical psychiatry. 7th ed. 1951.
Thorpe, W. V.: Biochemistry for medical students. 5th ed. 1952.
Tomkins, S. S.: Contemporary psychology. 1947.
Turner, A. L.: Diseases of the nose, throat and ear. 5th ed. rev. 1952.
White, P.: Heart disease. 4th ed. 1951.

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NEWS AND NOTES

Medical Society

The Coat of Arms for the Faculty of Medicine which was drawn up by Mr. A. Scott Carter, is now available to undergraduates and graduates in Medicine as a crest suitable for blazer wear and may be obtained at Henry Birks and Sons, Toronto, at a cost of ten dollars. Pins and rings in the same design are also available.

* * *

The Osler Society held its annual banquet on Thursday, February 5th. The members of the society were entertained after the banquet at the home of Dr. J. C. B. Grant, the Professor of Anatomy, who was the speaker and honoured guest for the evening.

* * *

The Medical Debating Society was the "government" in the U.C.–Meds Parliament on Tuesday evening, February 3rd. Lawler Loudon of Meds 5T5 and Paul Wolfish of Meds 5T8 spoke for the resolution "that education in the humanities without training in the sciences does not produce a mature mind." Apparently this combination of humanities and sciences is desirable among university students, because the resolution was upheld. This is the second interfaculty debate that the Debating Society has won this year.

* * *

The January meeting of the Medical Music Society dealt with opera. The subject was presented by Rita Ubriaco of Meds 5T6, who played selected recordings.

* * *

The Senior Meds team continues to hold down first place in Group I Interfaculty hockey. To date they have won four games, lost one game and tied one game. Helping to keep the team in the race for the Jennings Cup are: George DeVeber, Fred Walsh, Peter MacDougall, Don Marshall, and Robin Arnold of Meds 5T6, Ben Walker, Charlie MacDougall and (until he broke his arm) Bill Shaw of Meds 5T5, John Stalker, George Burrows, Stu Sims and John Keenleyside of Meds 5T4, Harry Hyde, Jim McGillivray, Gerry Cousins and John Dawson of Meds 5T3. Skip Kelly of Meds 5T6 is the manager and Peter Vernon of Meds 5T4 is the coach.

* * *

M.W.U.A.

Dr. Betty Stevenson entertained the women undergraduates with a tea at her home in Willowdale on Sunday, February 8th. Dr. Stevenson is the honorary president of the Medical Women's Undergraduate Association.

* * *

Faculty

A post-graduate course in Diabetes and Basic Metabolic Problems was conducted by the American Diabetes Association under the direction of Charles H. Best, C.B.E., M.D., F.R.S., on January 19th, 20th and 21st, 1953, at the University of Toronto.

* * *

A Refresher Course in Eye Surgery will be held in the Faculty of Medicine under the direction of the Department of Ophthalmology from April 13th to 17th. The guest surgeons will be Dr. Dohrinaun K. Piachel of San Francisco and Mr. H. B. Stallard, F.R.C.S., of London, England.

* * *

Alumni

The Medical Alumni Association has announced that it will make available in the spring of 1953, a scholarship or prize

of $300 to be awarded to a student at the end of the fourth medical year.

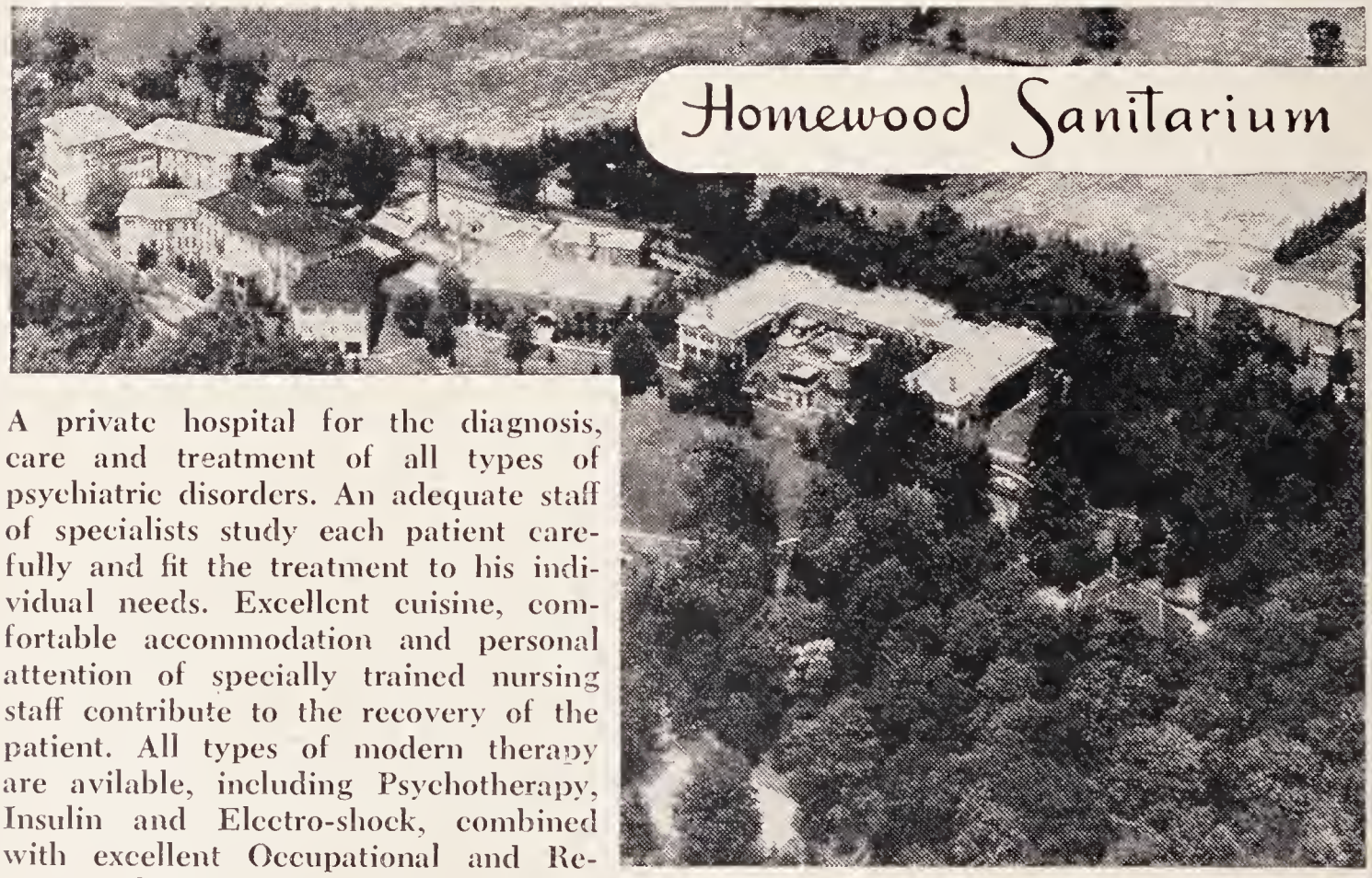
* * *

The annual "General Practitioner's Night" was held this year on January 31st before a very appreciative audience of Final Year students and internes. Dr. Stock very ably conducted the proceedings consulting the panel of experts on matters ranging from "The Fall and Rise of the G.P." to "Home Life for a Doctor". Guest speakers on the panel were:
Dr. Charlotte Hahn—the representative of the fairer sex on the panel, who is a general practitioner in Toronto.
Dr. Pearson—a Senior in surgery at Toronto Western Hospital who did 2 years of general practice with the Ontario Hydro.
Dr. Ives—an old-time country doctor from Stayner, Ontario.
Dr. Leeson—a young doctor in group practice in Cobourg, Ontario.
Dr. Waddington—a general practitioner in Toronto for 30 years.

For 2½ hours these speakers held the complete attention of this audience of Fourth Year students—a real tribute to their speaking ability! We are very grateful to them and also extend our thanks to Dr. Stock, Dr. Urquhart and Dr. Selby for their assistance in the evening.

* * *

A stated meeting of the Academy of Medicine, Toronto, was addressed by Harold G. Wolff, M.D., F.A.C.P., Head of the Departments of Neurology and Psychosomatic Medicine at the New York Hospital, Cornell Medical Centre in New York City, on Tuesday evening, February 3rd. His subject was "Headache Mechanisms."



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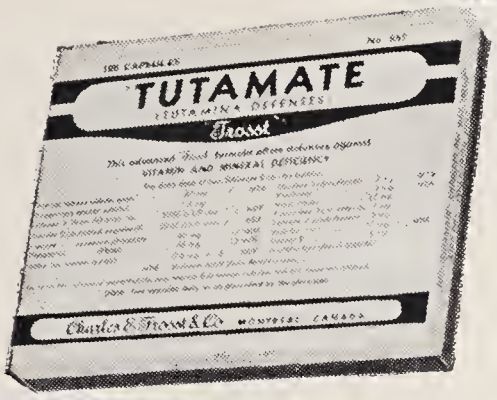

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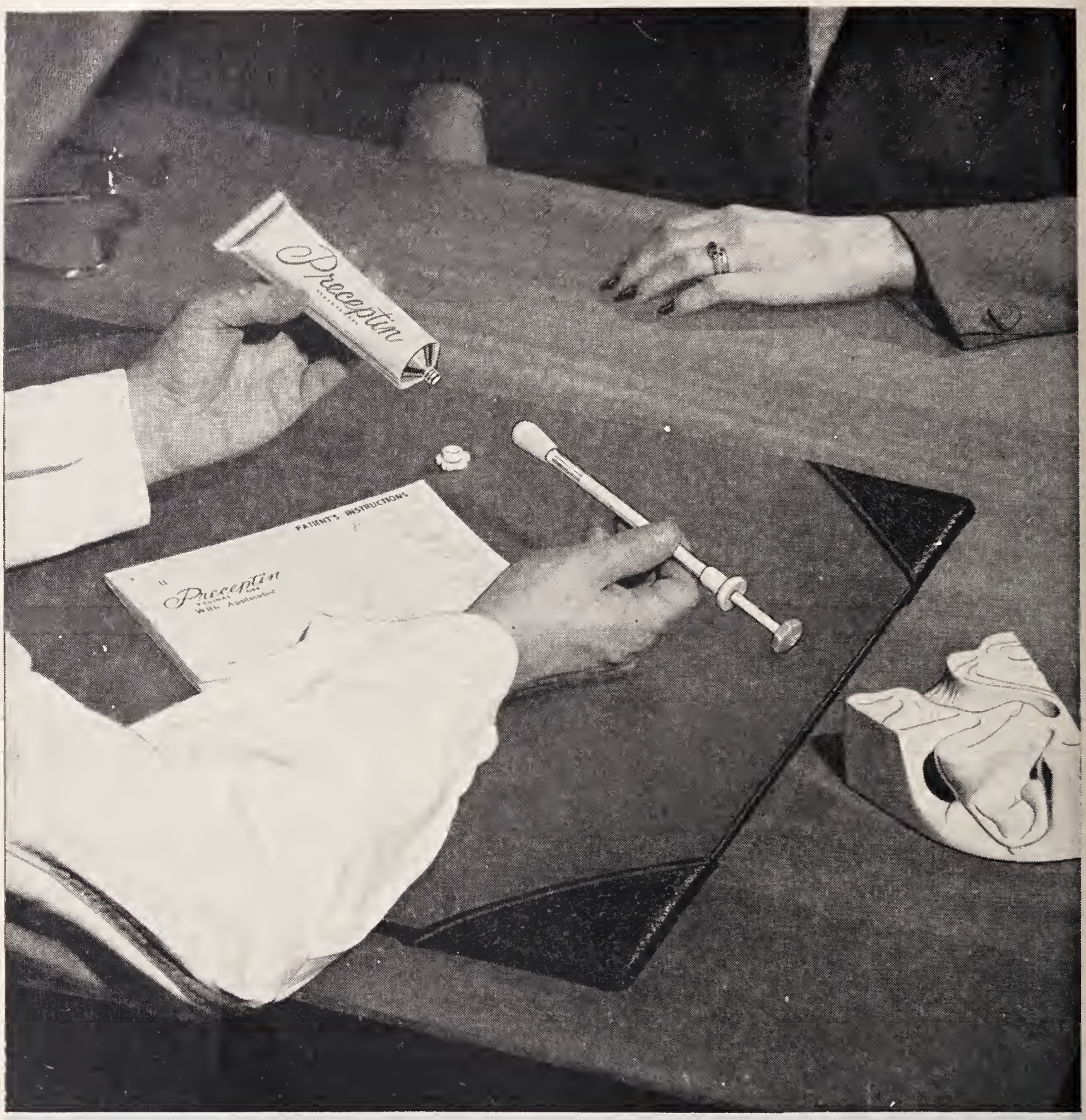

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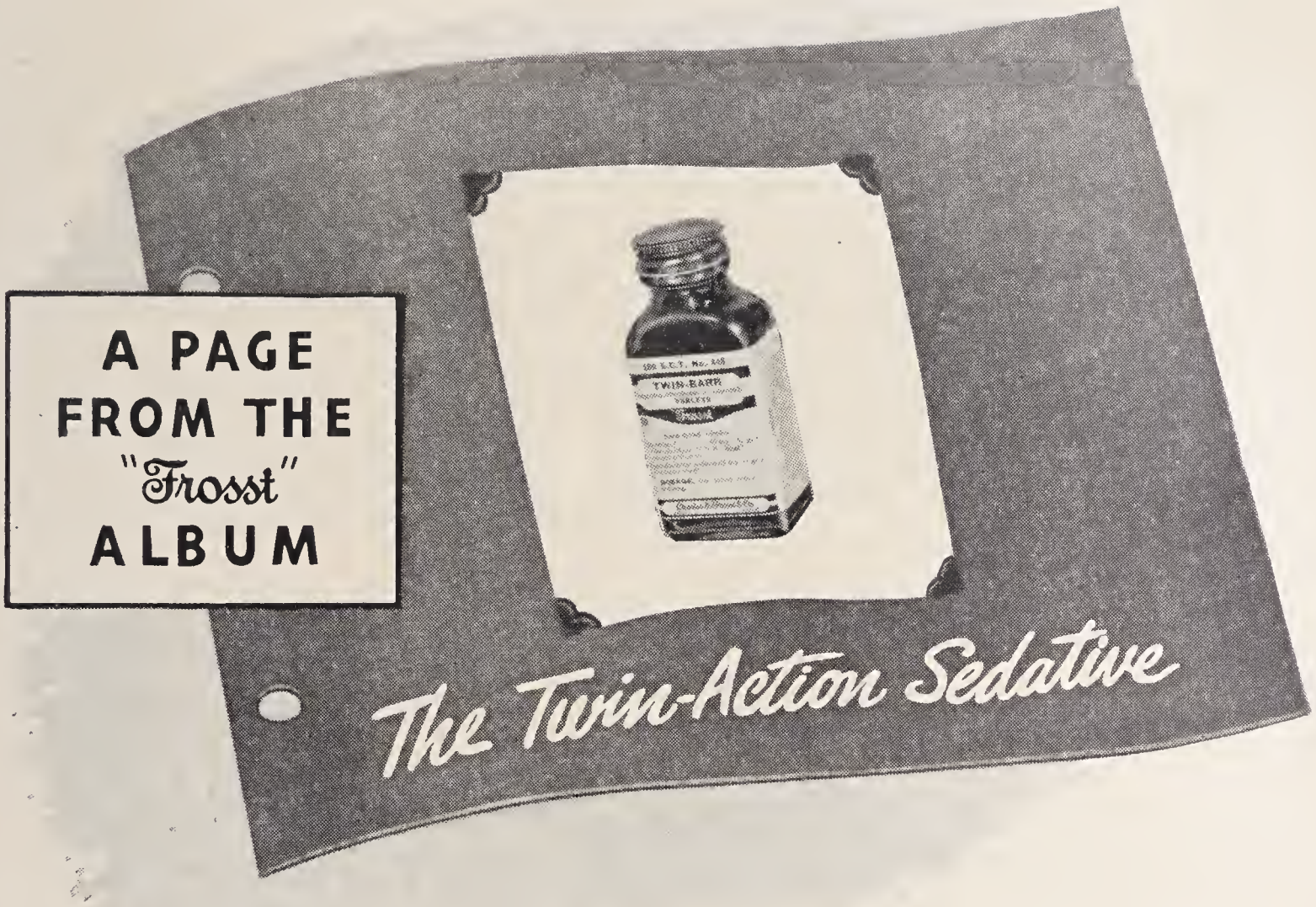

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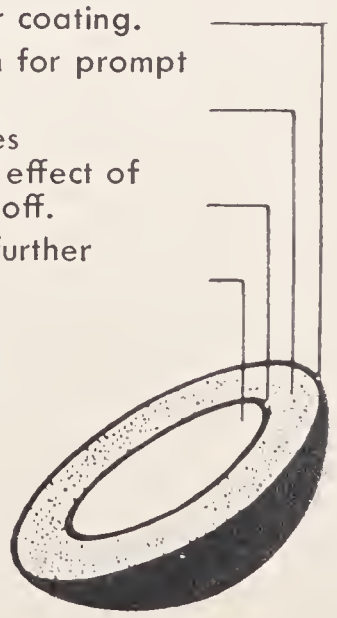

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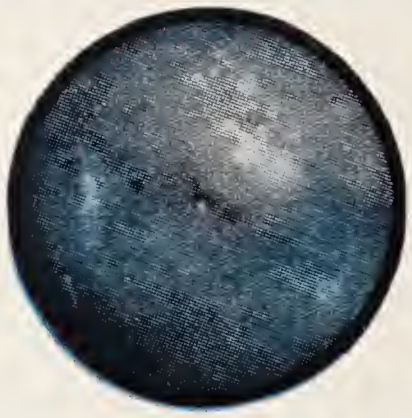

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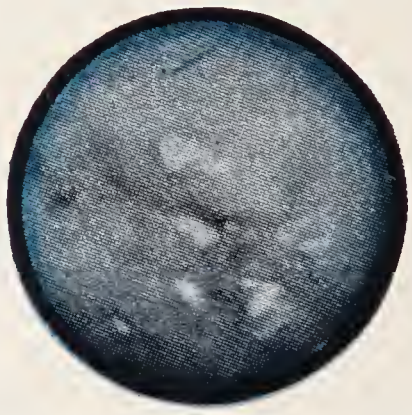

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√ Riboflavin	.250 mg.
√ Niacin	1.250 mg.
*Pyridoxine	.125 mg.
*d-Pantothenic Acid	.625 mg.
*Biotin	.001 mg.

*The significance of these vitamins in human nutrition is not yet established.

SUGGESTED DOSE: 8 cc. to 24 cc. (approximately 2 to 6 teaspoonfuls) daily as directed by the physician.

from natural rice bran source . . .
. . . plus added B factors

B•PLEX

Wyeth
Registered Trade Mark

ELIXIR VITAMIN B COMPLEX

Also available: B•PLEX CAPSULES
B•PLEX INJECTION

*Vitamin Therapy in General Practice: Edgar S. Gordon, M.D., M.A. and Elmer L. Sevringhaus, M.D., F.A.C.P.

NOW 3 "Farmer's Wife"

FORMULA MILKS

With these three types of "FARMER'S WIFE" milks you have a formula choice which simplifies the actual home preparation—insures more exact and constant milk formulae. All "FARMER'S WIFE" is Vitamin D increased to 480 International Units per pint, by the addition of pure Crystalline Vitamin D_3.

No. 1 Red Label—*Whole Milk. Butterfat 8%; Calories 45 per oz.*

No. 2 Blue Label—*Partly Skimmed Milk. Butterfat 4%; Calories 32 per oz.*

No. 3 Yellow Label—*Skimmed Milk. Butterfat 2%; Calories 29 per oz.*

● *Please write for professional information*

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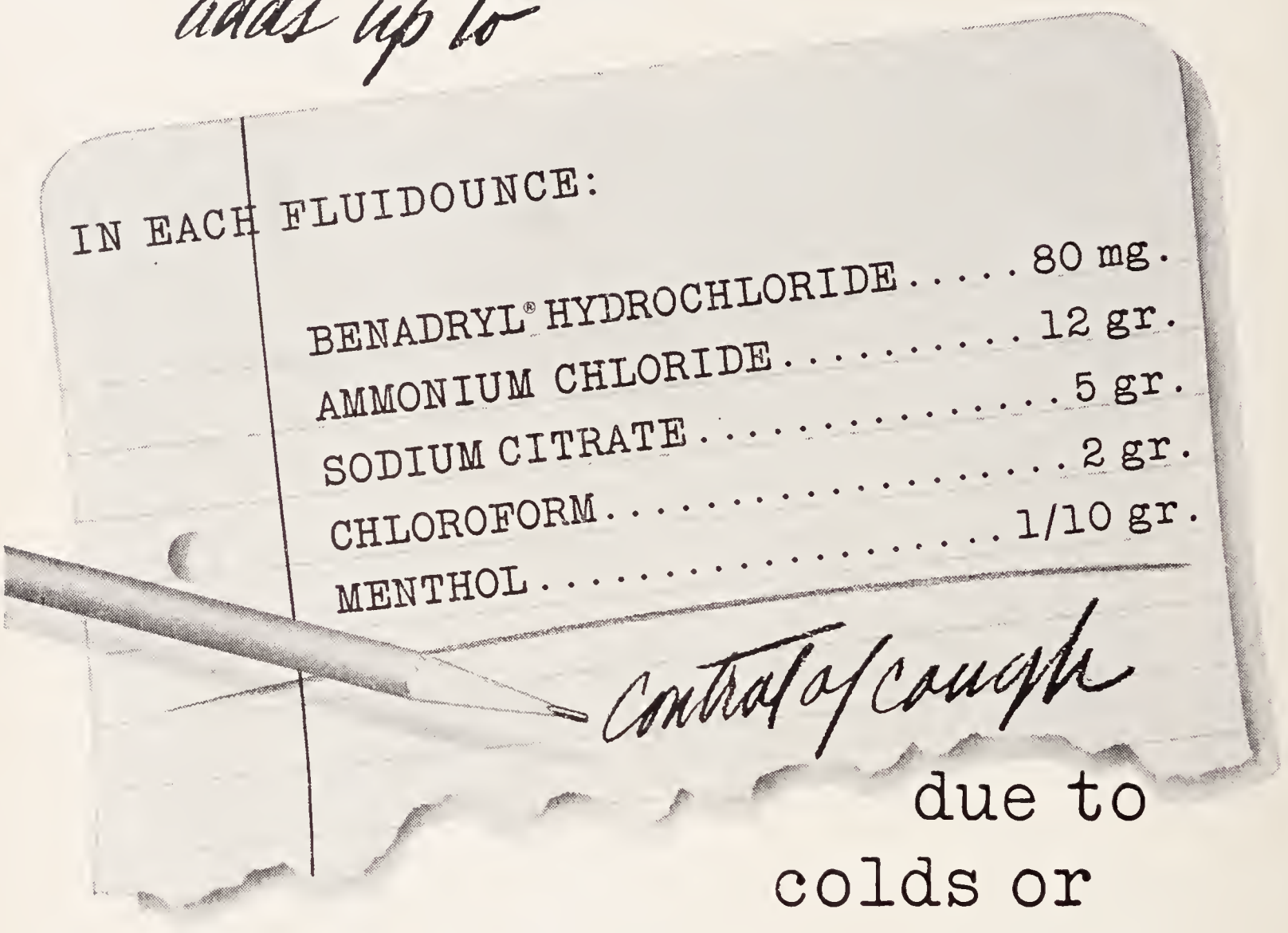
1-2B

Benylin® Expectorant

adds up to


IN EACH FLUIDOUNCE:
BENADRYL® HYDROCHLORIDE ..... 80 mg.
AMMONIUM CHLORIDE ..... 12 gr.
SODIUM CITRATE ..... 5 gr.
CHLOROFORM ..... 2 gr.
MENTHOL ..... 1/10 gr.

control of cough

due to colds or allergy

Because BENYLIN EXPECTORANT combines BENADRYL Hydrochloride — highly effective decongestant and antispasmodic — with established non-narcotic remedial agents, it provides rapid relief of cough. BENYLIN EXPECTORANT promotes patients' comfort by liquefying mucous secretions, relaxing the bronchial musculature, soothing irritated mucosae and relieving nasal stuffiness, sneezing and lacrimation. Patients of all ages like its mildly tart, raspberry flavor.

DOSAGE: One or two teaspoonfuls every two to three hours.
Children, one-half to one teaspoonful every three hours.
Supplied in 16-ounce, ½-gallon and 1-gallon bottles.

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